DEC 3 1985

507-G-20
94
COMPLETED

HE 20.3151/4:985

serial

Division of

CANCER PREVENTION & CONTROL

1985 Annual Report
October 1, 1984-September 30, 1985

ORIGI

U.S. DEPARTMENT
OF HEALTH
AND HUMAN SERVICES

National
Institutes of
Health

National
Cancer
Institute

Bethesda,
Maryland 20892

NCI
National Cancer Institute

Division of Cancer Prevention and Control

National Cancer Institute

Intramural Annual Report 1985

BLANK PAGE

Table of Contents

Page

Director's Report

Cancer Prevention Studies Branch

- Objectives
- Overview
- Accomplishments
- Plans
- Staff
- Bibliography

Biometry Branch

- Objectives
- Overview
- Office of the Chief
- Biostatistical Methodology and Cancer Control Epidemiology Section
- Clinical and Diagnostic Trials Section
- Screening Section
- Staff
- Bibliography

Surveillance and Operations Research Branch

- Objectives
- Overview
- Office of the Chief
- Operations Research Section
- Demographic Analysis Section
- Computer Systems Section
- Staff
- Bibliography

Appendix A

- DCPC Intramural Project Inventory
- Intramural Project Summaries (Forms PHS 6040)

BLANK PAGE

DIRECTOR'S REPORT

The National Cancer Institute (NCI) is expanding and accelerating an aggressive research and resources development program that reflects the Institute's mission and commitment to reduce cancer incidence, morbidity, and mortality. A specific goal has been set to reduce cancer mortality by 50 percent by the Year 2000.

Within the NCI, the Division of Cancer Prevention and Control [illegible]PC) is charged with the responsibility of directing cancer control activities. The Division emphasizes the continuum between research, technology transfer, and cancer control surveillance activities, with the DCPC research program aimed toward achieving measurable reductions in cancer incidence, mortality and morbidity, and increased cancer survival rates.

The DCPC consists of three major programs: Prevention, Centers and Community Oncology, and Cancer Control Science, each lead by an Associate Director. The Office of the Division Director provides overall coordination and direction and analytic program support. Within this organizational structure, Figure 1, three branches constitute the intramural program: Cancer Prevention Studies, Biometry, and Surveillance and Operations Research. This report briefly describes this intramural program with more details on each branch given in separate chapters.

Intramural research is essential to the National Institutes of Health activities. Development and conduct of research initiatives by NIH staff, along with the facilities and resources necessary to carry out these initiatives, which take advantage of opportunities particular to the federal government are important to the Cancer Control Program. Examples of some unique opportunities are those projects which involve international or interagency collaboration, require rapid access to specific high risk target populations and investigators engaged in common research areas, or necessitate methods development fundamental to the technical approach of many large-scale cancer control projects, including prototype models. The presence of an active intramural program also provides ready access to technical expertise relevant to scientific and management decisions made by extramural program directors. Thus, a coordinated program of intramural and extramural research on cancer prevention and control is a milieux which helps research proceed effectively.

The Cancer Prevention Studies Branch, located in the Prevention Program, contributes to the cancer control process by conducting controlled intervention studies. Intervention studies serve the dual pruposes of confirming hypotheses about cancer etiology and effecting cancer control, and act as a bridge between these two types of research efforts. The CPSB conducts intramural research in the areas of diet, nutrition and cancer, cancer chemoprevention, occupational cancer studies, or other cancer prevention strategies directed toward methods development and their application to lower human cancer risk.

The Biometry Branch, located in the Office of the Director, plans and conducts independent and collaborative studies in biostatistical and epidemiologic methodology and in mathematical modeling of processes relevant to cancer prevention and control activities. The Biometry Branch also provides consultation and review of proposed DCPC intramural and extramural projects concerning statistical methodology and study design.

The Surveillance and Operations Research Branch, also located in the Office of the Director, focuses on a broad range of analytic disciplines which support applications research and provide an assessment of the impact and achievements of cancer control programs. The SORB coordinates and directs analytic activities relevant to cancer control surveillance and monitoring progress toward cancer control in the United States, including geographically-based cancer reporting systems for cancer incidence and mortality, and program evaluation which assists the Director in establishing program priorities and resource allocation. The Branch also provides comprehensive computer systems support and applications research to the Division.

During the past fiscal year the Division implemented a major reorganization of the former Operations Research Branch and Biometry Branch to create the reconstituted Surveillance and Operations Research Branch and Biometry Branch. Subsequent to these changes the SORB moved from the intramural program to the extramural program to reflect the hybrid nature of SORB functions with the highest priority being placed on programmatic support while retaining a high level of independent and collaborative research initiatives.

These three units, and their interrelationships with other DCPC programs constitute the Division's intramural research program. This intramural program represents approximately 30% of the total DCPC staff and approximately 7% of the total DCPC budget for FY 85. The following chapters describe progress of the DCPC intramural program for FY 85. A brief summary of the Division of Cancer Prevention and Control follows and provides the program context in which intramural research is initiated and conducted.

The Prevention Program is charged with planning and supporting both intramural and extramural research in chemoprevention, diet and cancer, and cancer detection. In addition, this organizational unit serves as the focal point for coordinating diet, nutrition, and cancer activities across the NCI divisions.

The Centers and Community Oncology Program (CCO) supports shared research resources in cancer centers and applied research resources in the delivery of treatment, continuing care, and rehabilitation of patients with cancer. Within the Division of Cancer Prevention and Control, the CCO Program provides the framework for the integration of cancer centers and community activities. The CCO Program also has the responsibility of stimulating, developing, applying, and disseminating knowledge and technology related to cancer patient management.

The Cancer Control Science Program supports an integrated approach to cancer control research and applications. Program efforts are directed toward establishing cancer control as a scientific program where research on intervention strategies and their impact on populations is given primary attention.

The Office of the Director is responsible for the coordination and direction of the Division programs. It includes three branches: the Biometry Branch, the Surveillance and Operations Research Branch, and the Administrative Management and Planning Branch which assists in the management of the Division's budget and administrative matters. The Office of the Director is also responsible for coordinating the NCI-wide Smoking, Tobacco and Cancer Program.

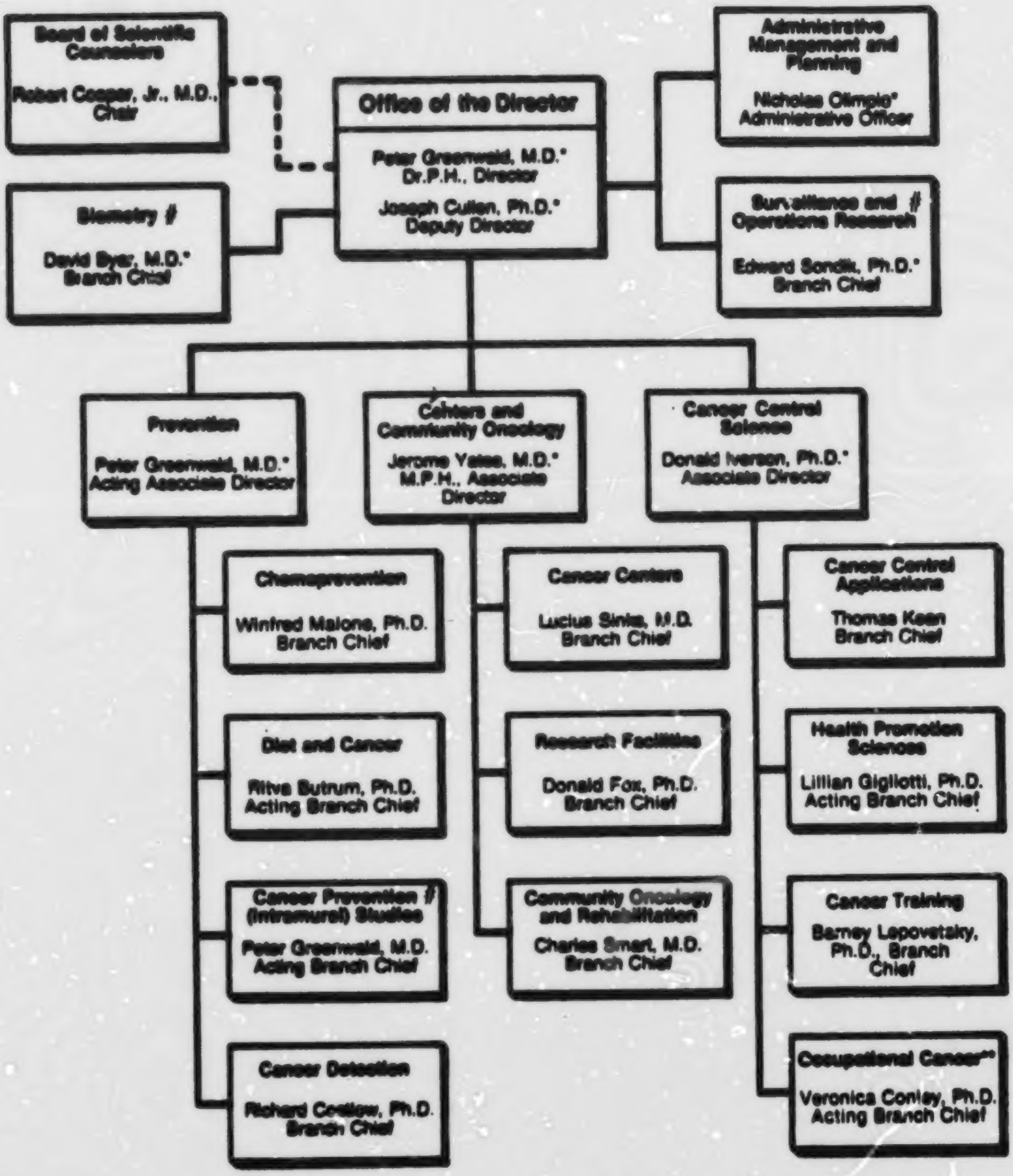
The intramural program described in the following chapters is composed of one branch within the Prevention Program and two branches within the Office of the Director: the Chemoprevention Studies Branch, the Biometry Branch, and the Surveillance and Operations Research Branch.

STAFF

Director:	Peter Greenwald, M.D., Dr.P.H.
Deputy Director:	Joseph W. Cullen, Ph.D.
Program Analyst:	Linda Bremerman
Program Director:	Thomas Glynn, Ph.D.
Program Director, Smoking Research Application:	James F. Callahan, D.P.A.
Special Assistant to the Office of the Director:	Margaret Mattson, Ph.D.
Program Development Officer:	J. Henry Montes
Program Staff:	Gayle Boyd,, Ph.D. Betty Lee Hawks, M.A.
Editorial Assistant:	Kathleen Y. Fanning Kathy Bauman
Secretarial Support:	Mary K. Gold Elizabeth Mugge M. Judith Uyehara Eve Scovel Zella Linn
Stay-In-School	Jose Ayala Sharon Gamble

Figure 1

Division of Cancer Prevention and Control Organization Chart


Board of Scientific Counselors
Robert Cooper, Jr., M.D., Chair
Office of the Director
Peter Greenwald, M.D.* Dr.P.H., Director
Joseph Cullen, Ph.D.* Deputy Director
Administrative Management and Planning
Nicholas Olimpio* Administrative Officer
Biometry #
David Byar, M.D.* Branch Chief
Surveillance and Operations Research #
Edward Sondik, Ph.D.* Branch Chief
Prevention
Peter Greenwald, M.D.* Acting Associate Director
Centers and Community Oncology
Jerome Yates, M.D.* M.P.H., Associate Director
Cancer Control Science
Donald Iverson, Ph.D.* Associate Director
Chemoprevention
Winfred Malone, Ph.D. Branch Chief
Diet and Cancer
Ritva Butrum, Ph.D. Acting Branch Chief
Cancer Prevention # (Intramural) Studies
Peter Greenwald, M.D. Acting Branch Chief
Cancer Detection
Richard Costlow, Ph.D. Branch Chief
Cancer Centers
Lucius Sinks, M.D. Branch Chief
Research Facilities
Donald Fox, Ph.D. Branch Chief
Community Oncology and Rehabilitation
Charles Smart, M.D. Branch Chief
Cancer Control Applications
Thomas Kean Branch Chief
Health Promotion Sciences
Lillian Gigliotti, Ph.D. Acting Branch Chief
Cancer Training
Barney Lepovetsky, Ph.D., Branch Chief
Occupational Cancer**
Veronica Conley, Ph.D. Acting Branch Chief

* Members of DCPC Director's Committee
** Transfer from Prevention Pending Approval
# Intramural Branch

Cancer Prevention Studies Branch

OBJECTIVES

The major objective of the Cancer Prevention Studies Branch (CPSB) is to contribute to the cancer control process by conducting controlled intervention studies. Intervention studies serve the dual purposes of confirming hypotheses about cancer etiology and effecting cancer control, and act as a bridge between these two types of research efforts. Controlled prevention trials are most effectively conducted when appropriate intervention strategies are applied to high-risk populations. Etiologic studies serve to generate and support hypotheses that help identify such strategies and populations. In this context, preliminary supporting or exploratory studies that establish the feasibility of doing such interventions, and ancillary research efforts that assist in explaining intervention study results, are also necessary.

OVERVIEW

The CPSB conducts intramural research in the areas of diet, nutrition and cancer, cancer chemoprevention, occupational cancer studies, and other cancer prevention stategies aimed at lowering human cancer risk. This specifically involves:

1. Planning, developing, and conducting nutritional and chemoprevention interventions and trials designed to test the effect of nutritional and chemopreventive agents in reducing cancer risk;

2. Determining the safety, toxicity, pharmacokinetics, bioavailability, and mechanisms of action of various potential chemopreventive agents;

3. Developing methods for assuring excellence in the performance of intervention studies; and

4. Analysis of dietary, genetic, and lifestyle components of data obtained from existing national screening surveys and other data bases to assist us in (a) understanding cancer etiology, (b) selecting appropriate intervention strategies, including both high-risk populations and agents, and (c) understanding complex interactions of various dietary factors in relation to cancer incidence and mortality.

ACCOMPLISHMENTS

The Branch has initiated 8 intramural projects in 3 broad areas, including prevention trials, etiologic studies, and exploratory/explanatory studies. These projects represent collaborative efforts in investigating dietary, nutritional, and constitutional factors relating to cancer prevention. Following is a brief summary of these 8 intramural projects, all but one of which will continue through and beyond FY 85.

Prevention Trials

U.S.-Finland Studies of Nutrition and Cancer (Z01 CN 00100 CPSB)

The important relationship of diet and nutrition in the development of cancer has become well known through various research efforts. Laboratory studies have shown cancer inhibitory function for various natural and synthetic nutrients in various models, which have been corroborated by human epidemiologic studies of nutrient intake, tissue levels, and cancer incidence. Vitamin A, beta-carotene, and selenium have been strongly implicated for their cancer preventive potential, with sufficient evidence for these substances to warrant their use in prevention trials. In addition, the roles of other nutrients in cancer cause and prevention (e.g., dietary fats and fiber) require further investigation.

The objectives of this cooperative project with the government of Finland are: (1) to determine if either beta-carotene or alpha-tocopherol supplementation is effective in preventing lung cancer in smokers; (2) to better assess the role of fats, selenium, and vitamins A,E, and C in breast cancer development; (3) to evaluate the relation of intake of various nutrients to subsequent cancer.

The project includes three studies. The first is a 5-year, randomized, double-blind, placebo-controlled, 2 x 2 factorial prevention trial of daily beta-carotene (20 mg daily) and alpha-tocopherol (50 mg daily) among smokers at high risk for lung cancer. The difference in lung cancer incidence between intervention groups will be determined. The second is a breast cancer case-control study of fats, total calories, selenium, and vitamins A,E, and C. The role of various anthropometric measurements as well as genetic markers for breast cancer will be explored. The third project will be a comparison of nutrient intakes in cases and references subjects identified from an existing large cohort with prediagnostic baseline dietary histories. Associations between various dietary components and several cancers will be assessed. Several pilot studies have been completed to date, and the prevention trial and breast cancer study are underway.

Use of Isotretinoin in Prevention of Basal Cell Carcinoma (Z01 CN 00103 CPSB)

This study is a 5-year, randomized, double-blind prevention trial designed to evaluate the effectiveness of low dosage levels of isotretinoin in reducing the incidence of basal cell carcinomas in a high-risk population, and to examine possible side effects associated with long-term administration of low doses of isotretinoin. Approximately 1200 evaluable subjects will be entered into the study within 18 months at 8 participating clinical centers located around the country. At each center, subjects will be randomly allocated to intervention (10 mg/day) or control (placebo) groups.

Vitamin A and its analogs, collectively known as retinoids, have been actively studied for several years in relation to their requirements in normal physiology and health, as well as for their potential in prevention of human disease. This vitamin is necessary for the differentiation of epithelial cells and is essential for the development and function of growth, reproduction, and vision. Deprivation or deficiency of vitamin A promotes tissue metaplasia and neoplasia in various animal and organ culture models. Supplementation with retinoids can reverse these changes and restore functions of cell growth and differentiation in various cell lines.

Laboratory experiments have shown that retinoids administered to animals can prevent chemical carcinogenesis. Since in most of the experiments animals were administered retinoids after their exposure to the carcinogen, the prophylactic effect of the retinoids is believed to be in the post-initiation phase, i.e., during promotion of carcinogenesis. In addition, several epidemiologic studies have shown an association of low dietary intake or serum levels of vitamin A with increased risk of cancer, notably lung cancer and other tumors of epithelial origin. Recent case reports have shown that isotretinoin can prevent the appearance of new basal cell carcinomas for four years in patients at high risk of developing new tumors.

Nutrition Intervention Study of Esophageal Cancer in Linxian, China
(Z01 CN 00112 CPSB)

The purpose of this project is to conduct two intervention trials using multiple vitamin-mineral supplements to evaluate the relation between such supplements and esophageal cancer mortality. One trial is being conducted in patients diagnosed with esophageal dysplasia (n = 3,400) and the other in the general population (n = 30,000). Participants for the dysplasia trial were screened and recruited in the Summer of 1984 and distribution of active pills initiated in May, 1985. For the general population trial, screening/recruitment will be accomplished during the Summer, 1985 with active pill distribution anticipated for the Fall, 1985. The studies will evaluate the effect of these supplements on regression/progression of esophageal dysplasia, total cancer incidence, total cancer mortality, and total mortality. These two studies are being conducted in Linxian (Henan Province) in the Peoples' Republic of China (PRC). Linxian, a rural county with population of 800,000, was selected because it has the highest rate of esophageal cancer in the world, and because there is suspicion that the population's chronic deficiencies of multiple nutrients may be etiologically involved.

This study is being conducted jointly by the Biostatistics Branch of the Division of Cancer Etiology and the Cancer Prevention Studies Branch of the Division of Cancer Prevention and Control at the NCI in collaboration with the Cancer Institute of the Chinese Academy of Medical Sciences.

Lung Cancer Intervention Study Among Yunnan Tin Miners - Feasibility Study

This pilot study will investigate the feasibility of conducting an intervention trial of micronutrients for the prevention of lung cancer among tin miners in Yunnan, China. The pilot will specifically be looking at general study logistics, ability to identify and recruit miners at high-risk, adherence to pill taking, potential adverse effects from intervention agents, quality control for data and sample collection/analysis, and baseline nutritional status among the miners.

Lung cancer rates are extraordinarily high among these miners. Males $\geq$ 40 years old with underground mining experience have a crude annual incidence of 1240×10^{-5} while miners aged 60-64 have an incidence rate in excess of 2500×10^{-5} annually. While the reasons for these high rates are not completely known, the miners have been exposed to a number of known carcinogens, including tobacco smoke, radon and radon daughters, and arsenic. In addition, dietary intake of several micronutrients are thought to be inadequate.

This study is being conducted by the Cancer Prevention Studies Branch in collaboration with the Department of Epidemiology of the Cancer Institute of the Chinese Academy of Medical Sciences, and the Labor Protection Institute of the Yunnan Tin Corporation.

Phase I Studies of Oral Synthetic Retinoids - 4-HPR (Z01 CN 00102 CPSB)

Phase I studies are needed to provide the parameters and characteristics of acute human toxicity, establish a maximally tolerated dose, delineate basic pharmacokinetics, and indicate a starting clinical dose for the investigational drug being developed.

Vitamin A and its synthetic analogs, collectively known as retinoids, have been actively studied in relation to their requirements in normal physiology and health, as well as for their potential in prevention of human disease, notably cancer. In this regard, it has been established that: (1) supplementation with retinoids can reverse tissue metaplasia and neoplasia in various laboratory models, restoring normal cell differentiation; and (2) retinoids administered to animals can prevent chemical- and viral-induced carcinogenesis. They have been repeatedly shown to delay the appearance, retard the growth, cause the regression, and prevent metastases of selected tumors. In addition, several epidemiological studies have shown an association of low levels of dietary and serum vitamin A and beta-carotene with increased risk of cancer.

Based on this evidence and case reports demonstrating successful chemoprevention of basal cell carcinoma with large doses of the retinoid isotretinoin, a Phase I intramural clinical trial of this promising new oral synthetic retinoid, 4-HPR (N-[4-hydroxyphenyl] retinamide), has been implemented with the objective of delineating the human toxicity patterns of orally administered 4-HPR.

Five patients in good general health but with multiple basal cell carcinomas initiated therapy at 800 mg/day. Toxicity was observed within 3 weeks in 3 different patients and further testing was discontinued.

Etiologic Studies

The Analysis of Long-Term Followup (LTF) Data from the Breast Cancer Detection and Demonstration Project (BCDDP)

The BCDDP screening program began in 1973 in 29 centers in 27 widely dispersed geographic areas of the United States. Initial screening was completed on over 280,000 women over a two-year period. From the original 280,000 participants in the screening phase of the BCDDP, approximately 64,000 were selected for 5 years of long-term followup (LTF) beginning in 1978, to assess the biology and natural history of breast disease, and to test hypotheses relating to detection, etiology, and survival. Those selected for LTF included all breast cancer cases found during the screening phase, all benign breast disease cases, all those recommended for biopsy, and a sample of "normals". The LTF data base will facilitate the exploration of important questions regarding the etiology and natural history of breast cancer. The size of the subcohorts and breadth of data available on them makes this population unique. The large number of cases of both breast cancer and benign breast disease with histologic information available should allow particularly useful analyses of several risk factors in relation these conditions.

The first 5 years of LTF will be completed in all centers by September, 1986. Further followup of the LTF subcohorts is anticipated.

NHANES I Epidemiologic Followup Survey: Chemoprevention/Nutrition Aspects (Z01 CN 00104 CPSB)

The purpose of the NHANES (National Health and Nutrition Examination Survey) Initial Epidemiologic Followup Survey was to conduct a longitudinal study of 14,407 adults originally surveyed in 1971-75, to investigate subsequent health and mortality outcome. Respondents were traced and re-examined. Information was obtained from hospital records, the National Death Index, and death certificates. The NHANES Initial Followup Survey was completed in 1984. The purpose of this intramural project is to examine the relation of chemopreventive, nutritional, and constitutional factors to cancer in the very large, representative population which NHANES offers. It provides an opportunity to examine these factors and potentially confounding or modifying factors in a prospective fashion, and to examine the effectiveness of dietary agents which are currently of great interest for cancer prevention. The relation of baseline vitamin use, biochemical or nutritional measures, and subsequent health status will be examined. A Continued Followup of the elderly (≥ 75 years old) in this cohort started in 1985, while the entire cohort will be followed up in 1986.

Exploratory/Explanatory Studies

Human Studies of Diet and Nutrition (Z01 CN 00101 CPSB)

The role of dietary factors in cancer prevention has been assessed in animal experiments, in human epidemiologic studies, and, most recently, in prevention trials. For many of these agents, however, information is incomplete concerning their safety, toxicity, dose, form, bioavailability, pharmacokinetics, and mechanism of action. To further define these parameters in humans, a cooperative research effort between the Beltsville Human Nutrition Research Center (BHNRC), U.S. Department of Agriculture, and the CPSB, DCPC, is being conducted. The overall goal of this collaborative effort is to obtain further information on potential cancer preventive agents. Initial efforts have focused on 3 nutrients which have shown the most promise for cancer prevention--selenium, fat, and beta-carotene.

A study of the kinetics of a single, oral dose of two forms of selenium in the fasting and non-fasting state was conducted in the first year. Future activities will evaluate the safety/toxicity of selenium and form of ingestion among persons residing in seleniferous areas.

Our first study of fat focused on potential mechanisms of action and will assist us in the evaluation of the relation of type and amount of dietary fat to hormonal status, bile acid metabolism, and fecal mutagenic activity in premenopausal women. Subsequent evaluations will examine the relation of dietary fat and fiber to fecal mutagens in men, focusing on the prominent mutagen, fecapentaene.

Beta-carotene studies are examining the plasma carotenoid response to single and long-term ingestion of beta-carotene from either a capsule or from selected vegetables.

PLANS

For the immediate future we expect to continue to consolidate the numerous activities that have been initiated by the Branch since its inception just 3 years ago.

We expect prevention trials to continue to be our major activity and we will continue to look for unique opportunities for trials, both within the U.S. and in foreign countries. Our focus will continue to be those cancer sites whose prevention will contribute the most to a reduction in cancer morbidity and mortality.

In the area of etiologic studies we will continue to work with existing data bases available to us. Within the BCDDP, we anticipate development of an approach to extend our observations on the existing long-term followup subcohorts. We will also be exploring the further study of women with especially severe family histories for breast cancer.

Explanatory/exploratory studies conducted collaboratively with the Beltsville Human Nutrition Research Center will continue for the immediate future to focus on the safety and form of selenium we ingest, the effect of varying types and levels of fat and fiber on fecal mutagens (in particular fecapentaene), and on the pharmacokinetics of carotenoids.

STAFF

Acting Branch Chief:	Peter Greenwald, MD, DrPH
Acting Deputy Branch Chief:	Philip R. Taylor, MD, SM
Pharmaceutical Study Coordinator:	Joseph A. Tangrea, MPH
Staff Fellows:	Demetrius Albanes, MD Christine Carter, PhD, MPH D. Yvonne Jones, PhD Marc S. Micozzi, MD, MSc Arthur Schatzkin, MD, DrPH
Research Associate:	Jan Morgan, RPh
Research Study Coordinator:	William Campbell, RN
Secretarial Support:	Felicia March Dorothy Trado

Cancer Prevention Studies Branch

Publications

Helzlsouer KJ. Selenium intoxication - New York. MMWR 1984;33:157-158.

Micozzi MS, Boone CW, Kelloff GA, Tangrea JA, Helzlsouer KJ, Taylor PR. Chemoprevention of cancer. Implications for clinical pharmacology. Journal of Clinical Pharmacology 1985;25(3):164-175.

Micozzi MS. Nutrition, body size, and breast cancer. Yearbook of Physical Anthropology 1985;28:(in press).

Tangrea JA. Recruitment: a perspective for multicenter clinical trials. Chemoprevention Clinical Trials - Problems and Solutions, November, 1984, NIH Publication No. 85-2715, p. 30-32.

Albanes D. Pilot studies: the U.S.-Finland project. Chemoprevention Clinical Trials - Problems and Solutions, November, 1984, NIH Publication No 85-2715, p. 78-79.

BIOMETRY BRANCH

OBJECTIVES

With the retirement of Dr. Earl Pollack as the Chief of the Biometry Branch (BB), an opportunity was provided for a reorganization of the Biometry and former Operations Research Branches, which had been considered appropriate for some time by the DCPC Director's Committee. Accordingly, the Demographic Analysis Section, which is responsible for the SEER Program, and the Computer Science Section were transferred to the newly named Surveillance and Operations Research Branch (SORB). The Screening Section was transferred form the old Operations Research Branch to the Biometry Branch. One new section was created in the reorganization, the Biostatistical Methodology and Cancer Control Epidemiology Section. The former Biometric Research and Analytic Studies Section of the Biometry Branch was dismantled because it was felt that the energies of the staff could better be used in other ways after the reorganization. The overall objectives of the newly reorganized Biometry Branch are summarized in the functional statement:

- "Plans and conducts independent and cooperative research studies concerning cancer epidemiology, prevention, screening, diagnosis, treatment, and control using methods of mathematical and analytic statistics;
- plans and conducts independent and collaborative studies in biostatistical and epidemiologic methodology and in mathematical modelling of processes relevant to cancer prevention and control activities;
- provides consultation and review of proposed projects concerning biostatistical methodology and study design to staff of the Division and to investigators in other divisions of NCI and outside;
- provides expertise in statistics and biometry to management and scientific decision-making meetings within the NCI and outside."

OVERVIEW

The work of the Branch is conducted via three Sections and by the Office of the Chief. The principal projects underway in each of these four organizational units will be described separately. The functional statements for each of the three sections will precede the description of their projects. Projects that involve collaboration across Sections or with the Office of the Chief have been placed arbitrarily in this report to avoid duplication. Because this has been a period of transition, special attention has been paid to continuing and finishing up work begun in the past while embarking on new projects more directly related to the newly identified functions. As time passes, further emphasis will be given to the projects most closely related to the program of DCPC.

OFFICE OF THE CHIEF

Year 2000 Projections

A comprehensive Fortran program has been written to project cancer mortality and incidence figures (numbers and rates) from 1980 through 2020 (Z01-CN-00142-01 SORB). The original idea for this project arose partly from work by Dr. David Eddy of Duke University who wrote a simpler program for a personal computer. The current program incorporates two different survival models (Weibull and mixed exponential), 40 cancer sites, the ability to begin with or without prevalent cases, temporal trends in underlying cancer incidence and in mortality from other causes, three possible interventions (primary prevention, screening, and treatment), age adjustment to the U.S. 1970 or 1980 population, calculation of annual incidence and mortality statistics, and comparison of these statistics under changing conditions of trends and interventions. Input to the model comes from various sources, and BB staff work closely with the SORB staff and have consulted with outside agencies including the U.S. Census Bureau, National Institute on Aging, and the National Center for Health Statistics. Work during the past year has included development and continued modification of the computer model based on discussion with potential users of the program, development of methodology for modelling cancer, and documentation of the program.

Community Intervention with Heavy Smokers

Extensive consultation has been provided to the staff of the Smoking, Tobacco, and Cancer Program concerning design issues which have arisen in the planning stages of a large-scale community-based study intended to promote smoking cessation among heavy smokers. Communities are to be paired and one community of each pair is to receive active intervention. Cluster sampling techniques and data from the Multiple Risk Factor Intervention Trial were used to determine the number of city pairs that would be required to obtain adequate statistical power.

Morbidity Among Long-Term Survivors of Childhood Cancer and Their Offspring (Z01 CN 00114-02 BB)

This study, done in collaboration with investigators in the Division of Cancer Etiology, was designed to detect the effects of cancer and its treatment on childhood patients who survived to adulthood, as well as any effects that might have been transmitted to their offspring. The study, a retrospective-cohort-with-sibling-control design, investigated the occurrence of subsequent primary cancers, quality of life, late morbidity other than cancer, infertility among the cases, and cancer and birth defects among offspring.

Cases selected from five U.S. cancer registries were patients under 20 years of age with a histologically confirmed malignant neoplasm or brain tumor diagnosis, and who reached the age of 21 years. Up to two sibling controls were selected for each case with sequential priority given to full blood relationship, same sex, closest in age. Interviewer-administered questionnaires were obtained for 2,285 (91 percent) cases and 3,265 (91 percent) controls.

Sixty one second primary cancers versus 17.3 expected (RR = 3.5, $p<0.01$) were identified among the 2,285 surviving cancer cases. A non-significant excess of cancers among the 3,265 sibling controls was observed (36 versus 26.7 expected).

In the Connecticut addendum to the main study, male survivors of childhood cancer were more often rejected from the armed forces, college and employment than their brothers. Females were significantly more likely than their sisters to be denied entrance into the military, but no differences were observed with respect to college or employment. Both sexes had more difficulty obtaining health and life insurance than their siblings. There was no excess among surviving cancer patients in the frequency of occurrence of major depressive episodes.

An addendum in Kansas to investigate availability of life and health insurance corroborated the Connecticut findings that surviving cases had significantly more difficulty in securing life or health insurance than their like-sex sibling controls.

BIOSTATISTICAL METHODOLOGY AND CANCER CONTROL EPIDEMIOLOGY SECTION

The responsibilities of this newly organized Section are summarized in its functional statement:

- "Plans and conducts independent and collaborative research concerning biostatistical and epidemiologic methodology related to cancer prevention and control;
- conducts or collaborates in the design and implementation of studies aimed at developing, refining, and testing hypotheses relating to applied cancer prevention and control, community oncology, and diffusion and adaptation of effective prevention, control, and treatment technologies;
- plans and conducts independent and cooperative studies into the theory and analysis of cancer prevention and control;
- provides statistical consultation both within and outside NCI to researchers concerned with problems related to Section responsibilities and staff expertise."

Research in Biostatistical Methodology and Mathematical Modeling
(Z01 CN 00121-01 BB)

Carcinogenic Models for Anti-cancer agents

The purpose of this project is to develop mathematical models of the cancer process which incorporate the action of cancer-inhibitory agents. These models are to be used to predict the effects to be expected in human intervention studies. The mathematical model being developed is derived from two-stage carcinogenesis models proposed by Armitage and Doll and by Moolgavkar, Venzon, and Knudson. These models presume that a normal cell is transformed into a malignant cell by two mutational events which occur only rarely. These models also assume proliferation of cells which have undergone the first mutation. The effect of anti-cancer agents is being modeled to act to inhibit either the cellular mutations or the proliferation of partially transformed cells. Each stage of action will predict different effects of intervention. The model being developed will be tested against the results of a human lung cancer case-control study which involves cigarette smoking as the primary carcinogenic exposure and vitamin A dietary intake as the anti-cancer agent of interest. The model will also be tested against the results of an experimental animal study involving carcinogenic exposure to DMBA followed by feeding of retinoids at different dietary levels after different delay periods before dietary intervention.

Models to Estimate Effect of Smoking on Lung Cancer

Lung Cancer has long been linked to the smoking of cigarettes. Epidemiologic and experimental evidence points to smoking having a carcinogenic effect at both an early stage and a late stage in the cancer process. The purpose of this project is to quantify the magnitudes of these two effects in order to derive optimal intervention strategies. The results of a large European multicenter case-control study of lung cancer were used to estimate the relative effects of cigarette smoking upon the initial and penultimate events in a presumed multistage cancer process. These estimates indicate that the predominant effect of cigarette smoking is upon a late stage in the development of lung cancer. In the future this project will be directed toward using these results along with information on age-specific smoking prevalence from the most recent Health Interview Survey to estimate the relationship between the historical prevalence of cigarette smoking in the U.S. to the recent mortality from lung cancer. The results of this analysis will be used to predict the quantitative effects on lung cancer mortality rates of hypothetical changes in the future prevalence of cigarette smoking.

Lung Cancer Mortality Trends

The purpose of this work is to project the future course of age-specific lung cancer mortality in the U.S. which would be expected if current trends persist without any specific population intervention. The statistical methods which are being used include logarithmic regression of historical age-specific mortality rates on calendar year as the independent variable, and use of an age-period-cohort model which relates mortality to an individual's age, his year of birth, and the calendar year of observation. The data being used for these analyses are the sex- and age-specific lung cancer mortality rates for 1958-1982. In both approaches the estimated trends will be projected into the future for each sex separately. The results from the age-period-cohort model approach indicate that lung cancer mortality first increased steadily with year of birth, reached a peak, and more recently is declining. The peak is thought to be caused by the changing prevalence of cigarette smoking by birth cohort. This model also indicates that mortality has been declining by calendar year after adjustment for the changes by birth cohort. The reason for this observation is unknown, but may be related to the changing tar content of cigarettes over this period. Work is continuing to compare various projection methods.

Logistic Regression Methodology

Current logistic regression methods for the analysis of retrospective case-control studies assume separate simple random sampling of cases and controls unrelated to prognostic variables of interest. However, population-based retrospective cancer studies involving differential sampling from multiple centers such as SEER registries are becoming more frequent and these centers are often related to environmental factors of possible etiologic significance, such as sunlight intensity or water supply. Using current regression methods it is difficult or impossible to estimate the relation between these factors and the cancer being studied. The purpose of this project is to derive a modified logistic regression method which incorporates knowledge of sampling rates used in different centers so that valid estimation is possible.

Interactive Time Trend Analysis Program

The purpose of this project is to develop a set of interactive computer programs permitting easy analysis of trends in cancer rates over time. One program will allow the user to define a particular Poisson regression model which includes effects for age, year of birth, calendar year of observation, sex, and race. A second program will allow the user to construct plots of age-specific mortality rates by calendar year or by year of birth, as well as plots of the various parameters in the regression models. The data used by these programs are U.S. sex-, race-, age-, and site-specific mortality rates for the period 1958-1982 (data for later years will be added when available), and international data collected by the World Health Organization which we obtained through the National Center for Health Statistics.

Descriptive Cancer Epidemiology (Z01 CN 00115-02 BB)

Trends of Mesothelioma Incidence in the U.S.

Recent trends in mesothelioma incidence rates from the population-based cancer registries in New York State (excluding New York City), Los Angeles County, and from the SEER Program have been studied. Results indicate a statistically significant increase in incidence during the period 1973-80 for pleural mesothelioma among white males but not for females nor for peritoneal mesothelioma for either sex. A panel of pathologists reviewed the cases from the New York State and Los Angeles County registries and concluded that the rising trend does not appear to be caused by changes in diagnostic practice.

Choriocarcinoma Incidence in the U.S.

Data from the SEER Program, the National Center for Health Statistics, and the Centers for Disease Control have been used to determine the incidence of choriocarcinoma in the U.S. An overall incidence of 1 per 25,000 pregnancies or 1 per 20,000 live births was determined. After adjustment for age and birth effects, race was found to have a significant effect with blacks and other races having twice the incidence of whites. However, these data do not permit separation of genetic and environmental contributions to the observed racial difference and further studies are warranted.

Prognostic Significance of Epstein-Barr Virus Antibody Titers in Nasopharyngeal Cancer Patients

Sequential serum samples from 100 Chinese patients with nasopharyngeal cancer have been tested for antibodies against several Epstein-Barr virus antigens. One sample was taken at diagnosis and up to 12 additional samples were taken every 3-6 months during follow-up. The prognostic significance of these antibody titers will be examined using survival analysis methods involving time-dependent covariates.

Excess Cancer Mortality in U.S. Counties

The purpose of this project is to identify counties in the U.S. which exhibit unusually high age-adjusted mortality rates for various cancer sites so that interventions may be designed to reduce disease occurrence. Thus far, mortality rates for lung, colorectal, prostate, breast, cervix, corpus, and ovarian cancer have been examined. Standard statistical methods for identifying "outliers" cannot be used since they assume a Gaussian probability distribution for the observations, an assumption contradicted by data for a number of the sites examined. We therefore identified counties with unusual mortality as those with age-adjusted rates which were significantly higher than the total U.S. rates for two recent time periods, 1976-78 and 1979-81, and for both sexes when not considering sex-specific sites. Future work in this area will include analysis of the incidence and survival experience for those identified counties where data are available, and extension of the analysis to other sites for which interventions may be feasible.

Nasopharyngeal Cancer Mortality Rates in the United States.

Geographic patterns of nasopharyngeal cancer mortality rates in the U.S. were examined using the system of economic subregions developed by the Bureau of the Census as the geographic unit of study. High rates among white males were found to be concentrated on the southeast Atlantic and Gulf coasts. This pattern was less evident in analyses based on smaller geographic units (state economic areas) and demonstrates the importance of selecting the most informative geographic unit for analyses of population-based incidence or mortality data. Nasopharyngeal cancer mortality rates for white males were positively correlated with cancer mortality rates of the respiratory tract, but not of the digestive system, at the economic subregion level. This suggests that inhalants rather than ingestants may be the predominant etiologic factor in nasopharyngeal cancer in this country.

Cancer in Oriental Populations (Z01 CN 00113-02 BB)

The Chinese and Japanese migrants to this country represent unique resources for epidemiologic investigations on cancer because the majority of them are concentrated in a few major settlements which facilitates comparison of their cancer experience with that of homeland populations. In accordance with the Division-wide cancer programs being conducted in the U.S. and abroad, studies of Chinese and Japanese were initiated to ascertain the transitional effect at both geographical and generational (nativity) levels. The results will help in designing strategies for cancer prevention and control programs for various populations and American-Orientals in particular and will increase our understanding of the marked variations in world-wide cancer incidence for particular cancer sites.

Cross-Continental Cancer Patterns

Studies on cancer among the Chinese in the U.S. have suffered in the past from the unavailability of comparable statistics on homeland populations. This limitation was largely resolved by the release of the 1975 People's Republic of China (PRC) national mortality survey data.

A study of cancer mortality among the Chinese in the U.S. by nativity and their counterparts in Hong Kong and Guangdong Province in the PRC was undertaken to ascertain possible migration effects, because the majority of American and Hong Kong Chinese migrated from Guangdong. Two distinctive patterns of displacement were discerned in relation to the site-specific risk-level noted for Guangdong and Hong Kong Chinese (GHC). For those cancers associated with high risk in the GHC population (nasopharynx, esophagus, liver, cervix and perhaps stomach), a downward transition was exhibited in American immigrant Chinese, with American born Chinese displaying even lower rates. In contrast, low risk cancers observed for GHC (colon, lung, breast, and leukemia) followed a different pattern, with foreign-born Chinese initially incurring a rise in mortality, and American born Chinese experiencing an intermediate risk between foreign-born Chinese and their homeland counterparts.

Based on a similar hypothesis of the first study, a second project was initiated comparing cancer mortality in Taiwan Province and Singapore with that for Fujian Province, since the majority of Chinese in the first two areas came from Fujian. Only small differences appeared for colon, rectum, uterus, and leukemia. For both males and females, stomach and esophagus showed excessive risk for Fujian as compared to Taiwan and Singapore, but lung cancer mortality rates were higher in Taiwan and Singapore than in Fujian. An attempt will be made in suggesting a conceptual frame of reference for the interpretation of the various site-specific similarities and differences between U.S. and Asian Chinese.

The study of Chinatowners in San Francisco and New York City was designed primarily to test the hypothesis that, in spite of the much noted differences in demographic and socioeconomic characteristics between Chinatowners and the general Chinese population, no consistent relationship exists between these attributes and health risks as reflected in the mortality profiles of the general Chinese population and Chinatowners. Preliminary findings seem to support the hypothesis as postulated. As a corollary proposition, the study intends to retest the findings of site-specific displacement in cancer mortality among the general Chinese population as documented in a previous study. Since the subjects in both studies share a common origin of birthplace, consistent results of both would therefore strengthen the implications of such findings for cancer control among U.S. Chinese.

Cancer Patterns in the U.S.

Incidence, mortality, and survival statistics on Chinese and Japanese groups in the SEER areas of San Francisco and Hawaii are being analyzed along with Los Angeles incidence data. Emphasis is placed on intercommunity differences as indicated below.

- Chinese: Geographic differences, most of long standing, were observed (e.g., higher rates in San Francisco than Hawaii for cancers of the lung, liver, and nasopharynx). Regardless of site-specific variations in risk level between Chinese and whites, the rank order of leading sites are similar (i.e., lung, colon and prostate for males, and breast, lung, colon, and corpus uteri for females).
- Japanese: Cancer risk differentials among the communities were reflected in generally higher rates in Hawaii than San Francisco (e.g., lung for both sexes, and stomach, prostate, bladder, thyroid, and liver among males). Though stomach cancer remains a much higher risk for Japanese than whites, the leading sites were similar for both: lung, prostate and colon among males and breast, colon, stomach (lung for whites), and corpus uteri among females.

Plans

For the U.S. Orientals, plans are being made to obtain 1980 data on Chinese and Japanese in the U.S. by nativity and in homeland areas, to extend the 1960 and 1970 cancer mortality analysis, thus permitting a two-decade trend analysis. The 1980 data are of particular interest because of the inclusion of a sizeable number of American born population at cancer ages. Attempts will also be made to secure local dialect data in Fujian, in order to compare them with those for different population segments in Singapore, and to discern more distinctive patterns of change in cancer mortality. The findings on site-community-specific differentials are being considered for initiation of studies of acculturation practices in relation to cancer prevention and control.

For the Chinese in China, data are being obtained to examine the relationship between esophageal cancer mortality and the chemical composition of soil and water samples in 7 counties of Hubei province, between hepatitis and primary liver cancer, and between dietary practices and stomach cancer in two high-risk areas. Testing of an innovative statistical method proposed by Chinese statisticians will be conducted using one set of data on cancer of the stomach. It is possible that findings emerging from these data will provide useful clues for initiating cancer prevention programs for U.S. populations in general and American Chinese in particular.

Development of Cancer Control Epidemiologic Methods (Z01 CN 00122-01 BB)

The purpose of this project is to develop the methodology of cancer control epidemiology, with emphasis on its conceptual foundations in biological, statistical, and epidemiological theory. Research areas include: concepts of cause and prevention; the logic of epidemiologic inference, the structure of causal and preventive models, the relationship of biological models of carcinogenesis to causal and preventive models and to models of interactions, problems of self selection and selection bias, the role of case-control methodology in studies of early detection, and the scientific, technological and ethical implications of cancer control epidemiology. Some specific examples of work underway in this project include:

Studies in Causal and Preventive Inference

Strong inferences and valid conclusions are important to any scientific study, but they are especially important in cancer control epidemiology, because results may be translated directly into practice as preventive measures. In this project, an examination of the forms and uses of logic in cancer control epidemiology is underway. Two specific areas of inquiry are the use of inductive and deductive logic in epidemiologic explanations, and the problem of causal criteria.

In the first of these areas, the origin, consistency, testability and permanence of epidemiologic explanations are being examined in terms of inductive and deductive logic. In this work the concept of refutability has emerged as being of particular importance. In practical terms this means that when considering a variety of testable hypotheses, that explanation of the data from a study which best survives attempts at refutation is logically to be preferred.

In the second area of inquiry involving the use of logic in epidemiology, the problem of causal criteria is being examined in terms of a critical deductive method. Hypothesis-dependent criteria include strength of association, biologic gradient, temporality, preventability, consistency, and specificity. Other criteria such as plausibility and coherency were shown to be related to predictability and testability. The problem of how epidemiologists decide to act on the basis of research results requires a comparative examination of three basic decision techniques: belief, probability, and criticism. It appears that criticism is the most important.

Studies in Causal and Preventive Interactions

The role of interaction in epidemiologic research is controversial. At least three categories of interaction have been identified: biological, statistical, and public health. A general examination of the links between these categories of interaction was undertaken in order to define these ideas more precisely. It was concluded that although simple statistical models of interaction are testable, limiting attention to additive and multiplicative models alone may be inadequate unless they can be tied to more explanatory biological theories. A study of mathematical models of carcinogenesis is underway with the goal of deducing simple statistical models of interaction between two or more preventive agents or between causal and preventive agents. For both the multistage theory and the initiation-promotion model of Moolgavkar, a multiplicative model of interaction is deduced. Implications for testing such biological models are being developed.

Selection Bias and Generalizability

Selection bias may interfere with the generalizability of results drawn from intervention studies, whether they are controlled clinical trials or "observational" studies, because the results from studies on highly selected groups may be the only data available for predicting the effects of applying interventions to large populations. One example of this kind of selection is the healthy worker effect. In order to understand this effect better, the mortality experience of a large nationally distributed population of communications workers was compared to the general U.S. male mortality. Mortality rates were much lower for the communications workers. Examination of death rates by duration of employment and age revealed that the deficit in mortality increased with the age of the worker and for a given age, was greater for those employed for short periods compared to medium or long periods. It was concluded that both selection at entry and selection later during employment are involved in these effects. In the course of this work it was noted that some confusion in characterizing selection effects in occupational populations is accounted for by the use of trends in rate differences in some studies and trends in rate ratios in others.

CLINICAL AND DIAGNOSTIC TRIALS SECTION

The overall objectives of the Section are summarized in its functional statement:

- "Engages in independent and cooperative research on statistical methodology for design of controlled clinical trials of cancer prevention and treatment and for field testing of diagnostic techniques;
- provides full statistical support in selected trials, including development of the detailed study plan, supervision of data collection, processing, and editing, and analysis of the data as well as preparation of scientific papers;
- develops statistical techniques for analyzing trial results, for identifying prognostic factors and diagnostic determinants, and for analyzing observational data;
- consults and collaborates extensively with other researchers requiring expertise in these and related areas."

Statistical Methodology Research (Z01 CN 00116-02 BB)

Sample Size Calculations

A program to compute power and sample size for a variety of experimental design situations has been written to operate interactively on the NIH DEC-10 computer system. The user may specify the total time patients are accrued in a trial, length of followup time after patient accrual is completed, extent of drop-in or drop-out of patients from assigned treatment groups, stratified designs, a lag time until treatment is expected to work, and patient loss to follow-up. The program is user friendly and prompts for answers to design questions. Optional user instructions provide a description of program capabilities as well as citing the literature from which equations used in the calculations were adapted. Future capabilities will include power calculations for one and two sample problems comparing means, proportions and correlations as well as those for matched and unmatched case-control studies.

Development of Sample Size Determination Methodology for Prevention Trials

Existing methods of sample size estimation are being adapted for planning cancer prevention trials. Subjects entering these trials may have preexisting cancers and thus not be susceptible to the intervention. Including such cases as trial outcomes will underestimate the true intervention effect. Prescreening before trial entry may remove some of these cases. Since no screen is perfect, their effect can be mitigated, but not eliminated. It appears that in the context of prevention trials, sample size will always have to be increased; the greater the dilution effect, the greater the increase in sample size at the planning stage.

Methods of calculating sample size to compensate for the dilution effect have been developed for trials where the proportions test is appropriate. Expected event rates are dependent on estimates of disease prevalence, incidence in the screened population, screening test sensitivity and specificity. The cases of Poisson rates and survival analysis (using the Mantel-Haenszel test) will be considered.

Another aspect of this project is the development of a cost model which allows overall assessment of the costs of screening compared to the costs of a larger sample. Consideration will be given to the costs and benefits of combining screening and prevention trials.

Simplified Sample Size Estimation for Prevention Trials

The low expected event rates in prevention trials allow conventional equations for sample size to be replaced by simpler approximations. Such approximations are useful because they are accurate and computationally simple. These methods are being applied to common complicating features of trial design such as failure of compliance, stratified design, and delayed onset of treatment effectiveness.

Partial Factorial Designs

Work on factorial designs for prevention studies has continued, particularly the investigation of the new class called partial factorial designs in which certain cells are deliberately omitted from full balanced factorial designs either because of anticipated toxicity or ethical considerations. It has been found that such designs offer advantages over fractional factorial designs and though less efficient than full balanced factorial designs nevertheless permit estimation of most quantities of interest.

Tests for No Treatment Effect in Randomized Clinical Trials when Balanced Covariates are Missing

Standard computer analyses of clinical trial data may yield anticonservative significance tests for no treatment effect if needed covariates are omitted from statistical models even if such covariates are perfectly balanced across treatment groups. Permutational variances have been shown to be appropriate in this situation and are suggested instead of variances based on the information matrix. Fortunately, two commonly used models, the logistic and Cox models, are not seriously affected by these considerations.

Error in Variable Problems

Extending the work of Carroll et al. (1984, Biometrika), maximum likelihood procedures have been developed for estimating parameters in generalized linear models as well as other models when covariates are subjected to errors in variables (structural models). Score tests for no treatment effects when covariates are subjected to errors in variables are also developed. This work was motivated by the need for appropriate methods for analyzing data from studies of nutrition and diet since appreciable variation in measurement can be expected in such studies.

Statistical Analysis of Proportional Odds Models in Survival Analysis

Proportional odds models have recently been applied to survival analysis by Bennett (1983a Appl. Stat., 1983b Statist. in Medicine) and Pettitt (1984 Appl. Stat.). In this research both Bayesian and empirical Bayesian approaches are adopted to develop confidence ellipsoid for parameters. An infinite series is developed such that the first term is the classical asymptotic maximum likelihood solution. Currently we are applying the results to the Veteran's Administration Lung Cancer Data to illustrate the procedure.

Multievent Model of Carcinogenesis with Stochastic Birth and Death Processes

The Moolgavkar-Knudson (Moolgavkar and Knudson 1981 JNCI) two-stage stochastic birth-death model of carcinogenesis is extended to a multi-stage stochastic birth-death model of carcinogenesis. Biological evidence for this model is provided by the experimental results of Lands et al's experiments on cotransfection of ras and myc oncogenes in nude mice (Lands et al. 1983 Nature). For studying cancer intervention and control by stochastic multievent models, the results of Tan and Gastardo (1985 Math. Biosciences) is also extended to multistage models with stochastic birth and death processes.

Stochastic Gompertz Birth-death Process

It is well known that growth of many types of malignant tumors is best described by Gompertz growth curves (Laird 1969, NCI Monograph 30, Simpson-Herren and Lloyd 1970 Cancer Chemother. Rep. Part 1). To date, only deterministic Gompertz growth is available. This research extends deterministic Gompertz growth to stochastic Gompertz birth-death process.

Stochastic Logistic Growth Models

Deterministic logistic growth has been used extensively to describe normal and tumor cell growth in carcinogenesis (Eisen 1979, Lecture Notes in Biomath. No. 30, Springer-Verlag). To describe stochastic growth of cells, this research extends the deterministic logistic growth to stochastic logistic processes. The first four cumulants of the process are approximated. A diffusion process approximation is derived. Using this result, the absorption probabilities, the mean absorption, the mean absorption times and the variance of first absorption times to detectable tumor size and/or tumor regression are derived.

Consultation on Clinical Trials and Other Studies (Z01 CN 00119-02 BB)

Lung Cancer Clinical Trials

The Section provides full statistical support for the Lung Cancer Study Group. This group of seven major medical centers was formerly supported by contract with the Division of Cancer Treatment (DCT), but has been successful in competing for continued support under a cooperative agreement. The activities of the group include 9 protocols in lung cancer and accrual of some 350 patients per year. The primary emphasis of these protocols is the study of adjuvant chemotherapy, radiotherapy, or immunotherapy in patients with resected lung cancer. Currently, patients are accruing to seven protocols, four protocols are in the followup phase, and four replacement protocols are being developed. Results from several of these protocols provide evidence that combined chemotherapy (cytoxan, adriamycin, cis-platinum) may prolong survival in patients with non-small cell lung cancer. A study of adjuvant intrathoracic BCG in patients with resected non-small cell lung cancer revealed no benefit from this form of immunotherapy. Radiotherapy is under investigation in several protocols. Recently, protocols have been developed to evaluate the role of surgery following a course of chemotherapy and/or radiotherapy designed to render inoperable patients inoperable. The role of surgical resection following induction chemotherapy in small cell lung cancer is being investigated in collaboration with the EORTC.

Looking for Cancer "Hotspots"

This project was started in response to questions about geographic areas which have unusually high or low survival experience, or an unusual distribution of stages at diagnosis. Standard statistical methods have been adapted to answer this question. In certain cases, aggregating data from several geographic regions is necessary in order to provide sufficient cases for survival calculations. This procedure has been formalized. SEER survival experience for colon and breast cancer has been used to answer substantive questions about areas with outlying survival experience and the need for further investigation. For both cancers mentioned, several SEER areas have been identified as possible outliers. These techniques will be applied to other common cancers such as lung, uterus, and an aggregate of all cancers thought to respond favorably to treatment.

Analysis of Cancer Maps

The use of maps of cancer mortality has been commonplace, but special statistical methods are needed to deal with problems inherent in analyzing these aggregated data. In particular, geographic regions represent observations which are not independent due to the shared environment of neighboring areas. We have used linear regression for the analysis of mortality maps, accounting for correlated observations with a spatial difference term which can be used as an explanatory variable. Using lung cancer in white males and data for state economic areas, we identified variables possibly related to variations in lung cancer mortality which closely match those identified by other methods. These techniques are being applied to data on prostate and other cancers, in order to generate hypotheses about environmental causes of cancer.

Selenium Pharmacokinetics Study (Z01 CN 00107-03 BB)

Selenium is a possible cancer preventive agent, and is being considered for use in intervention trials. A study in collaboration with the Cancer Prevention Studies Branch (Z01 CN 00101 CPSB) is in progress which will provide information on the pharmacokinetics of selenium in its prototype forms -- sodium selenite (inorganic form) and selenomethionine (organic form). This information is unavailable for these agents in the doses currently considered optimal, and it is necessary for the determination of time and manner of administration. Parameters such as percent absorption, maximum concentration, time to maximum concentration, and mean residence time will be estimated for a single dose and compared in fasting and non-fasting subjects.

Population Consumption of "Protective" or "Harmful" Foods

In order to carry out prevention programs aimed at reducing cancer incidence through dietary modifications, it is necessary for policy-makers to have a clear picture of the current American diet. A study examining the consumption of specific foods and food groups in the American diet, focusing on those foods thought to be harmful or protective with respect to the development of cancer, is underway in collaboration with the Surveillance and Operations Research Branch (Z01 CN 00111-02 SORB) and the National Center for Health Statistics. The study uses twenty-four hour dietary recall data collected in the second National Health and Nutrition Examination Study (HANES II). Individual HANES II food codes were combined into food groups; the choice of groups was based on the literature on diet and cancer and the interim dietary guidelines of the National Research Council report in Diet, Nutrition and Cancer. Foods under study which are thought to be protective include fruits, vegetables (all garden, cruciferous, deep yellow and leafy green), fruits and vegetables high in vitamin A or high in vitamin C, and breads and cereals high in fiber. Foods considered potentially harmful include red meat and meats containing nitrites (bacon, hot dogs, luncheon meats). Consumption of poultry and fish is also being investigated. The analysis is being done by sex, race (white, black), broad age group (19-29, 30-54, 55+), poverty index (by tertile) and region (Northeast, South, Midwest, and West). As HANES II data comprise a representative national sample, national estimates may be made of the proportions of Americans consuming foods in the above groups. For example, preliminary estimates show that less than 60 percent of the population ate any vegetable (excluding potatoes and salad); the proportion eating any cruciferous vegetable was only 13 percent. Data from the HANES II food frequency questionnaire will be used to amplify and corroborate the above analysis.

Serum Markers for Breast Cancer

Serum and background information have been collected from over 12,000 women for evaluation of biological markers for breast cancer. Shipments of blinded panels of serum were sent on request to qualified researchers during the past year. Several investigators used monoclonal antibodies in attempting to discriminate among sera from control, benign and breast cancer groups. Others studied CEA, lipid bound sialic acid or ductal carcinoma antigen as potential markers. When the results of the assays of blinded sera are completed, the data are returned to the Clinical and Diagnostic Trials Section for analysis, and these analyses and unblinded data are returned to the investigators.

Black vs. White Survival for Prostate Cancer

Data from the VACURG prostate studies were analyzed to assess the importance of race as a prognostic factor for survival when considering death due to cancer or death from any cause. After adjusting for the known prognostic factors including tumor grade, acid phosphatase, metastases, age, tumor size, ureteral dilatation, and treatment, race was not a significant indicator of prognosis in the patients with extended disease. However, the distributions of patients across these detailed disease status indicators show that the blacks are likely to have a more extensive disease at diagnosis than the whites.

The National Death Index

The National Death Index (NDI) offers an efficient method of ascertaining mortality and subsequently determining cause of death for the large numbers of persons involved in studies conducted or funded by the NCI. Potential application of the NDI to a broad spectrum of programs in DCPC has been explored. Efforts to acquaint investigators in the prevention community with the NDI and its uses were begun in the 1984 fiscal year and have continued in 1985. A joint NCI-NCHS colloquium, "Overview of the National Death Index and Experiences of Users", held in 1984 was followed by a presentation, "Use of the NDI", at the Prevention Clinical Trials Workshop in May, 1985. A paper aimed at potential NDI use in the cancer research studies was made available in the last fiscal year and is currently being prepared for publication in collaboration with the National Center for Health Statistics.

A working group consisting of a representative from each of the five NCI Divisions has been formed to explore the feasibility, content and implementation of an Institute-wide policy.

SCREENING SECTION

The overall objectives of the Section are summarized in its functional statement:

- "Plans, conducts and analyzes independent and cooperative research studies in screening for the early detection of cancer;

- conducts methodologic research in statistics, probability and epidemiology with particular emphasis on techniques appropriate to the design, analysis and modeling of randomized and observational studies in cancer screening and related areas;

- engages in independent and cooperative research to determine cancer natural history and risk characteristics of populations for application to the design and interpretation of early detection and related studies;

- maintains liaison with other agencies, organizations and professional societies concerned with cancer screening and related methodology in order to coordinate and optimize activities."

Studies in Cancer Screening (Z01 CN 00106-02 BB)

Data from several cancer screening studies are being collected and analyzed to gain a better understanding of the impact and consequences of such screening in various population settings. The results can be used by NCI in establishing cancer control policy. These data bases also provide an opportunity for the development and testing of new techniques for data analysis. The studies fall into three categories: randomized trials, international working groups, and occupational cohorts.

Randomized Trials

Three large scale randomized trials have been conducted by NCI to evaluate screening for breast, lung and colorectal cancer. Staff participate in the scientific, and in some cases, administrative conduct of these studies. The HIP breast cancer screening trial is now in its 22nd year and is nearing completion of the long term follow-up phase of the trial. This study has demonstrated a 30 percent reduction in breast cancer mortality as a result of screening with physical examination and mammography. It has also spawned several subsidiary analyses such as lead time estimation, and served as the basis for NCI policy and studies in other countries. Analysis of the final data base will focus on the magnitude and duration of the benefit, age-specific effectiveness and the independent contribution of each screening test. The lung cancer trial conducted at Johns Hopkins University, Memorial Sloan Kettering Hospital and the Mayo Clinic was brought to a successful conclusion during this year. The results indicate that screening for lung cancer with chest X-ray and sputum cytology does not result in a reduction in lung cancer mortality in the population of high risk heavy smokers studied. The colorectal cancer screening trial at the University of Minnesota is currently in progress to evaluate the Hemoccult test for blood in the stool. Staff participate in scientific consultation and ongoing data monitoring for this study.

International Working Groups

Participation on two international cancer screening working groups has continued this year. The working group on cervical cancer screening of the International Agency for Research on Cancer has analyzed data from cervical cancer screening programs in Scandinavia, Scotland, Canada, and Italy. The aim has been to develop data useful for deciding the optimal ages and intervals for screening by estimating disease natural history parameters through their relationship to cervical cancer incidence rates following negative screens. Results of this study, based on certain assumptions such as 100 percent attendance, indicate that the maximum achievable reduction in cervical cancer risk for women aged 20-64 is about 90 percent with annual screening starting at age 20. An 80 percent reduction can be achieved with screening every five years starting at age 25. The screening evaluation project of the International Union Against Cancer conducted a workshop on screening for gynecologic cancers, emphasizing cervical cancer. It was concluded that in developed countries, where resources are available, screening every three years provides practically the same benefit as annual screening, that screening should begin at age 25 in most populations, and the same screening frequency should be used irrespective of age.

Occupational Cohorts

Screening in two high risk occupational cohorts is under investigation. In collaboration with the Division of Cancer Etiology (DCE), data from the bladder cancer screening program at the DuPont Company are being analyzed to relate disease characteristics and outcome to urine cytology and blood tests, smoking history, and exposure to benzidine and beta-naphthylamine. The tests are being evaluated as indicators of exposure, predictors of disease, and for their possible impact on disease outcome through early detection. With DCE and the National Institute of Occupational Safety and Health, current follow-up data are being collected for a study of sputum cytology screening for lung cancer among uranium miners in the western United States. The relationships among cytology classification, radiation exposure, smoking history, lung cancer and mortality data will be analyzed.

In addition to the above projects, staff have been involved in various advisory and consultative roles at NCI during the year. Subject areas have included examination of screening for melanoma and cervical cancer, and advising on uses of data and data analysis for the Breast Cancer Detection Demonstration Projects. Consultation was also provided on sample size requirements and protocol design for a study of the sensitivity and specificity of a monoclonal antibody marker test for ovarian cancer. Staff have also participated in developing the NCI-wide Detection and Diagnosis Plan.

Research in Cancer Screening Methodology and Modeling (Z01 CN 00105-02 BB)

The focus of this project is the development and refinement of statistical procedures for the design and analysis of cancer screening and related studies. Statistical problems under investigation include sample size determination, development and comparison of data analysis methods, and development of monitoring procedures and stopping rules for screening trials. Each of these problem areas is common to screening and prevention trials in which the Division participates, but the methods for screening studies must address the special lead time and length biases inherent in screening programs.

Sample Size Calculation

Methods of sample size calculation are being investigated for estimating sensitivity, specificity or predictive value of a screening test and comparing these properties between two tests. A procedure based on a statistical test for paired data has been developed for the situation where two tests are performed on a group of subjects and individuals positive on either test receive a diagnostic work-up. The second category of study is the screening trial in which one population receives the screening test and another serves as a control. Here procedures are being developed which account for the time after the start of a study before the effect of screening on mortality begins to appear.

Lead Time and Length Bias

Research into methods to estimate and adjust for lead time and length bias have continued. Survival data in breast cancer screening are being analyzed to attempt to isolate lead time, length and selection bias components and the relative role each plays in creating a spurious screening effect. A method to adjust survival data of screen detected cases for lead time has been developed under the assumption of independence between lead time and survival time. Extensions to the correlated situation are being pursued.

Analysis of Mortality in Screening Studies

A new approach to the analysis of mortality data in screening studies was developed to examine whether breast cancer screening produces a delay in mortality or a long term cure for screen detected cases. The theory of competing risks was used to analyze case survival data from the HIP study. Survival from time of study entry was used to eliminate lead time bias and length bias was avoided by analyzing case groups comprising all cases diagnosed up to the point after screening stopped at which the numbers of cases in the control group equaled that in the screened group. It was concluded that some breast cancer cases detected early as a result of screening realized a benefit in terms of cure, that is, elimination of the risk of breast cancer mortality.

Stopping Procedures for Screening Trials

Whereas in most therapy trials the question is whether to stop early or continue for a predetermined time, in screening and other prevention studies the preclinical disease natural history and interaction with the intervention are usually not well understood, so that another option is to extend a study beyond the termination date. The focus of the present research is to use cost-benefit methodology to determine, at successive time points, whether to stop or continue a study. A Baysian approach of updating prior information with newly acquired data is used.

Other Research

Staff attempt to remain abreast of developments in mathematical and simulation modeling of cancer screening, primarily for cervix, breast, lung and colorectal cancer. For colorectal cancer, creation of a screening model has been initiated. The model must account for two potential sources of benefit from screening with sigmoidoscopy or an occult blood test. One is the early detection of cancer which might result in improved survival for such individuals. The second is the detection and removal of polyps which could lead to reduced incidence and thereby reduced mortality from colorectal cancer. Initial efforts will utilize a computer simulation model developed by Dr. Knox in England. Extensions to analytic models and other simulation approaches will be addressed.

In recent years, case-control studies have been suggested for use in evaluating screening programs and a few such studies have been done for cervical and breast cancer screening. At issue are the accuracy and applicability of this design in the screening setting. Research to examine case-control studies within screening randomized trials is underway. A comparison of the screening effect as indicated by case-control studies will be made against the randomized trial standard. Alternative definitions of cases, controls and exposure periods will be assessed, and the impact of various matching variables will be analyzed.

BIOMETRY BRANCH STAFF

Office of the Chief

Branch Chief	David P. Byar, M.D.
Senior Investigator, C.O.	David L. Levin, M.D.
Mathematical Statistician	Max H. Myers, Ph.D.
Secretary	Gloria E. Fleming
Clerk-Typist	Varnetta A. Bush

Biostatistical Methodology and Cancer Control Epidemiology Section

Section Head	Charles C. Brown, Ph.D.
Statistician	Roger R. Connelly, M.S.
Research Sociologist	Haitung King, Ph.D.
Statistician	Frances B. Locke, M.S.
Epid. Trainee	Bruce Trock, Ph.D.
Senior Staff Fellow	Douglas Weed, M.D., Ph.D.
Secretary	Caroline Ball

Clinical & Diagnostic Trials Section

Acting Section Head	David P. Byar, M.D.
Computer Systems Analyst	Donald K. Corle, M.S.
Statistician	Blossom Patterson, M.A.
Senior Staff Fellow	Steven Piantadosi, M.D., Ph.D
Expert	Wai Yuan Tan, Ph.D.
Secretary	Julie Paolella

Screening Section

Section Head	Philip Prorok, Ph.D.
Statistician	Robert Connor, D.Eng.
Epidemiologist	Janet Sobell, M.S.
Staff Fellow	Stuart Baker, Sc.D.
Secretary	Gayle Marwine

BIOMETRY BRANCH BIBLIOGRAPHY

Aron, J.L., and Prorok, P.C.: An analysis of the mortality effect in a breast cancer screening study. Int. J. Epidemiol. In press.

Brown, C.C.: High to low dose extrapolation of animal carcinogenesis studies. In Proceedings of the Twenty-ninth Conference on the Design of Experiments in Army Research, Development and Testing. Research Triangle Park, North Carolina, U.S. Army Research Office, ARO Report 84-2, 1984, pp. 329-354.

Brown, C.C.: Statistical aspects of the estimation of human risks. In Woodhead, A.D., Shellabarger, C.J., Pond, V., and Hollaender, A. (Eds.): Assessment of Risk from Low-Level Exposure to Radiation and Chemicals. New York, Plenum Press, 1985, pp. 125-140.

Bruzzi, P., Green, S.B., Byar, D.P., Brinton, L.A., and Schairer, C.: Estimating the population attributable risk for multiple risk factors using case-control data. Am. J. Epidemiol. In press.

Byar, D.P.: Assessing apparent treatment covariate interactions in randomized clinical trials. Statistics in Medicine. In press.

Byar, D.P.: Sample size considerations for prevention studies. In Sestili, M. (Ed.): Chemoprevention Clin. Trials. U.S. Department of Health & Human Services, NIH Publication No. 85-2715, Washington, D.C., U.S. Government Printing Office, 1984, pp. 14-19.

Byar, D.P.: Statistical analysis techniques and sample size determination for clinical trials of treatments for bladder cancer. In Prout, G.R., Niijima, T., Schroder, F., and Denis, L. (Eds.): EORTC GU Group Monograph Series. In press.

Byar, D.P., and Piantadosi, S.: Factorial designs for randomized clinical trials. Cancer Treat. Rep. In press.

Connelly, R.R., and Levin, D.L.: Temporal Changes and International Differences in Pancreatic Cancer Incidence. Proceedings of the International Symposium on Pancreatic Carcinoma. Ulm, Germany, 1983. In press.

Corle, D.K., Sears, M.E., and Olson, K.B.: Relationship of quantitative estrogen-receptor level and clinical response to cytotoxic chemotherapy in advanced breast cancer: An extramural analysis. Cancer 54: 1554-1561, 1984.

Curtis, R.E., Kennedy, B.J., Myers, M.H., and Hankey, B.F.: Evaluation of AJC stomach cancer staging using the SEER population. Semin. Oncol. 12: 21-31, 1985.

Devesa, S.S., Horm, J.W., and Connelly, R.R.: Trends in lung cancer incidence and mortality in the United States (Chapter 3). In Mizell, M., and Correa, P. (Eds.): Lung Cancer: Causes and Prevention. Deerfield Beach, Florida, Verlag Chemie International Inc., 1984, pp. 33-45.

Dillard, T.A., Piantadosi, S., and Rajagopal, K.R.: Models for prediction of ventilation at maximum exercise in patients with chronic airflow obstruction. Am. Rev. Resp. Diseases. In press.

Gail, M.H.: Applicability of sample size calculations based on a comparison of proportions for use with the logrank test. Contr. Clin. Trials. In press.

Gail, M.H.: Book Review: Clinical Trials: A Practical Approach by S. Pocock. Contr. Clin. Trials 6: 84, 1985.

Gail, M.H.: Nonparametric frequentist methods for monitoring comparative survival studies. In Krishnaiah, P.R. (Ed.): Handbook of Statistics. Amsterdam, North Holland Publishing Company. In press.

Gail, M.H.: The evaluation of serial marker measurements for monitoring patients at risk of recurrent cancer. In Mastromarino, J. (Ed.): The Biology and Treatment of Colorectal Cancer. Martinus Nijhoff Publishing Co. In press.

Gail, M.H., and Byar, D.P.: Variance calculations for direct adjusted survival curves. Biometrical Journal. In press.

Gail, M.H., and Simon, R.: Testing for qualitative interactions between treatment effects and patient subsets. Biometrics. In press.

Gail, M.H., Lubin, J.H., and Silverman, D.T.: Elements of design in epidemiological studies. In Eisenfeld, J. and DeLisi, C. (Eds.): Mathematics and Computers in Biomedical Applications. Amsterdam, North Holland Publishing Company, 1985, pp. 313-323.

Gail, M.H., Wieand, S., and Piantadosi, S.: Biased estimates of treatment effect in randomized experiments with non-linear regressions and omitted covariates. Biometrika 71: 431-444, 1984.

Gastwirth, J.L., and Gail M.H.: Simple asymptotically distribution-free methods for comparing Lorenz curves and Gini indices obtained from complete data. Advances in Econometrics. In press.

Goedert, J.J., Biggar, R.J., Winn, D.M., Mann, D.L., Byar, D.P., Strong, D.M., DiGioia, R.A., Grossman, R.J., Sanchez, W.C., Kase, R.G., Greene, M.H., Hoover, R.N., and Blattner, W.A.: Decreased helper T lymphocytes in homosexual men. I. Sexual contact with high-incidence areas for the acquired immunodeficiency syndrome. Am. J. Epidemiol. 121(5): 629-36, 1985.

Goedert, J.J., Biggar, R.J., Winn, D.M., Mann, D.L., Byar, D.P., Strong, D.M., DiGioia, R.A., Grossman, R.J., Sanchez, W.C., Kase, R.G., Greene, M.H., Hoover, R.N., and Blattner, W.A.: Decreased helper T lymphocytes in homosexual men. II. Sexual practices. Am. J. Epidemiol. 121(5): 637-44, 1985.

Green, S.B., and Byar, D.P.: Using observational data from registries to compare treatments: the fallacy of omnimetrics. Statistics in Medicine 3: 361-370, 1984.

Greenwald, P., Costlow, R., Prorok, P., and Sondik, E.: Screening in the Context of Cancer Control. In Miller, A.B. (Ed.): Screening for Cancer. New York, Academic Press, Inc., 1985. In press.

Heise, H.W., Myers, M.H., et al.: Recurrence-free survival time for surgically treated soft tissue sarcoma patients: Multivariate analysis of five prognostic factors. Cancer. In press.

Holmes, G.E., Baker, A., Hassanein, R.S., Bovee, E.C., Mulvihill, J.J., Myers, M.H., and Holmes, F.F.: The availability of insurance to long-time survivors of childhood cancer. Cancer. In press.

Interdisciplinary Panel on Carcinogenicity (C. Brown, member): Criteria for evidence of chemical carcinogenicity. Science 225: 682-687, 1984.

King, H., Li, J.-Y., Locke, F.B., Pollack, E.S., and Tu, J.-T.: Patterns of site-specific displacement in cancer mortality among migrants: the Chinese in the United States. Am. J. Public Health 75: 237-242, 1985.

Krewski, D., Brown, C., and Murdoch, D.: Determining "safe" levels of exposure: safety factors or mathematical models? Fund. Appl. Toxicol. 4: S383-S394, 1984.

Lawrence, C.E., Taylor, P.R., Trock, B.J., and Reilly, A.A.: Trihalomethanes in drinking water and human colorectal cancer. JNCI 72: 563-568, 1984.

Levine, P.H., and Connelly, R.R.: Epidemiology of nasopharyngeal cancer. In Wittes, R.E. (Ed.): Head and Neck Cancer. Sussex, United Kingdom, John Wiley and Sons Ltd. In press.

Levine, P.H., Connelly, R.R., and McKay, F.W.: Burkitt's Lymphoma in the United States: Cases reported to the American Burkitt Lymphoma Registry compared with Population-Based Incidence and Mortality Data. In Lenoir, G., O'Connor, G.T., and Olweny, C. (Eds.): Burkitt's Lymphoma: A Tumor Model. IARC Sci. Pub. In press.

Mason, T.J., Costlow, R., and Prorck, P.C. (Eds.): Proceedings of the NIOSH/NCI/EPA Conference on Medical Screening and Biological Monitoring in the Workplace. J. Occupational Med. In press.

Mason, T.J., Prorok, P.C., Neeld, W.E., and Volger, W.J.: Screening for bladder cancer at the DuPont Chambers Works: initial findings. J. Occupational Med. In press.

Morrow, J.S., Levin, D.L., et al.: Placental proteins as tumor markers in human monoclonal gallopathies: Results in 109 patients. Tumour Biology. In press.

Piantadosi, S.: A model of growth with first order birth and death rates. Compar. Biomed. Res. 18: 220-232, 1985.

Piantadosi, S., Byar, D.P., and Gail, M.H.: Screening geographic areas for unusual survival experience or stage at diagnosis with application to breast and colon cancer. JNCI. In press.

Prorok, P.C.: Methodologic Issues in Randomized Controlled Trials of Screening. In Prorok, P.C., and Miller, A.B. (Eds.): *Screening for Cancer I.: General Principles on Evaluation of Screening for Cancer and Screening for Lung, Bladder, and Oral Cancer*. UICC Technical Report Series, Volume 78. Geneva, 1984, pp. 18-28.

Prorok, P.C., and Miller, A.B. (Eds.): *Screening for Cancer I.: General Principles on Evaluation of Screening for Cancer and Screening for Lung, Bladder, and Oral Cancer*. UICC Technical Report Series, Volume 78. Geneva, 1984, 186 pp.

Slud, E.V., Byar, D.P., and Green, S.B.: A comparison of reflected versus test-based confidence intervals for the median survival time based on censored data. *Biometrics* 40: 587-600, 1984.

Tan, W.Y.: Bayesian approach to robust procedures for ANOVA models under heteroscedasticity and nonnormality. *Sankhy B.* In press.

Tan, W.Y.: On first passage probability distributions in continuous time Markov processes. *Utilitas Mathematica*. In press.

Tan, W.Y.: On Tiku's robust procedure -- A Bayesian insight. *J. Statist. Plan. and Infer*. In press.

Tan, W.Y.: Multivariate filtered Poisson processes and applications to multivariate stochastic modelling of mutagenicity and carcinogenesis. *Utilitas Mathematica* 26: 63-77, 1984.

Tan, W.Y., and Gastardo, M.T.C.: On the assessment of effects of environmental agents on cancer tumor development by a two-stage model of carcinogenesis. *Math. Biosci*. In press.

Weed, D.L.: An epidemiologic application of Popper's method. *J. Epidemiol. Community Health*. In press.

Weed, D.L., and Trock, B.J.: Criticism and the growth of epidemiologic knowledge. (letter to the Editor). *Am. J. Epidemiol*. In press.

SURVEILLANCE AND OPERATIONS RESEARCH BRANCH

OBJECTIVES

Overall objectives of the newly formed Surveillance and Operations Research Branch are summarized in its functional statement. The Branch focuses on a broad range of analytic disciplines which support applications research and provide an assessment of the impact and achievements of cancer control programs. The Surveillance and Operations Research Branch:

- Plans, directs, coordinates, and evaluates a program of research on analytic methods, surveillance techniques, operations research and computer systems research and services for the Division;
- conducts research and develops quantitative methods for monitoring progress toward cancer control in the United States;
- coordinates a number of geographically-based cancer reporting systems which collect and maintain cancer incidence and mortality data bases, and provides routine and special reports and analyses from the data bases relevant to cancer control surveillance;
- provides comprehensive operations research and program evaluation support and guidance to the Division by developing the data and providing scientific interpretation of the data and related evidence, assists the Director in establishing program priorities and integrating projects of the Division and its interrelation with other NCI divisions; and
- advises the Division Director and supports activities of the National Cancer Advisory Board and other scientific advisory committees on cancer prevention and control related surveillance, analytic, and operations research activities.

OVERVIEW

The Surveillance and Operations Research Branch (SORB) is organizationally located in the Office of the Director, Division of Cancer Prevention and Control (DCPC). The SORB includes the Office of the Chief and three Sections: Operations Research, Demographic Analysis, and Computer Systems.

On April 25, 1985, the former Operations Research Branch and the Biometry Branch were officially reorganized according to plans proposed and approved by the DCPC Director's Committee. Out of this reorganization came the SORB with its reconstituted functional units. The Demographic Analysis Section, which has primary responsibility for the Surveillance, Epidemiology, and End Results (SEER) Program was transferred from the Biometry Branch. The Computer Science Section in the Biometry Branch was absorbed into the Computer Systems Section to bring under one organizational unit these diverse technical support and research activities. Lastly, a new Section was created, the Operations Research Section, to encompass analytic activities related to cancer control program planning and management, resource allocation, economics, and program evaluation. The former Screening Section was moved into the Biometry Branch and the former Biostatistics Section was abolished.

Reorganization of the Surveillance and Operations Research Branch was much more than mere rearrangement of Sections and their existing function. The SORB expanded its mission to be consistent with the NCI emerging Cancer Control Program, focusing its primary role on bridging the gap between cancer control research and application. Branch activities are most clearly characterized as the scientific study of operating systems and administrative structures which enable findings to be put to practical use quickly. Of major importance was the decision in late FY '85 to change the Branch status from intramural to extramural. This decision was based primarily on the hybrid nature of Branch activities which cut across all the DCPC extramural as well as intramural programs, where the highest priority is programmatic support, yet retain a high level of research initiatives within these interactions.

Work of the Branch is carried out in six broad program areas which span the Office of the Chief and the three Branch Sections through linkages to the Centers and Community Oncology Program, the Cancer Control Science Program, and the Prevention Program. These six program areas are: cancer control surveillance, operations research applications, program planning and evaluation, computer systems development, research data management, and dietary assessment research. In this report each of these six areas will be discussed separately, within the context of one of the functional units which is most closely allied with the program activity.

OFFICE OF THE CHIEF

OBJECTIVES

The Office of the Chief plans, directs, and coordinates the Branch program, including establishing Branch policies, developing budgets, assigning available resources, and integrating Branch activities within NCI and NIH, outside of NIH, and with other Federal and non-Federal agencies, on a nationwide basis. Coordination of several major cancer control activities occurs within the Office of the Chief: Year 2000 Cancer Control Objectives Cancer Control Surveillance Plan, Annual Cancer Control Statistics Review, National Center for Health Statistics - National Cancer Institute Coordinating Committee, program evaluation, and data management and implementation of large-scale intervention trials. Several projects are also provided with analytic direction by senior staff members in the Office of the Chief.

YEAR 2000 CANCER CONTROL GOALS AND OBJECTIVES

The NCI is establishing a set of national cancer control objectives aimed at guiding the cancer control effort toward the overall goal of reducing cancer mortality by 50 percent by the Year 2000. Cancer control objectives are defined as quantitative changes in cancer incidence, mortality, and other appropriate measures of the cancer burden. These objectives help the NCI make decisions for cancer control program directions, set priorities for allocating resources between competing uses, and evaluate program progress.

The analysis for setting the objectives is being performed by members of the cancer control research and practice communities and NCI staff. A final report is in preparation for the National Cancer Advisory Board. This report is organized into four strategic areas: prevention, cancer screening and detection, treatment, and cancer control surveillance. In cancer prevention, quantified objectives are developed for public knowledge and behavior related to diet, nutrition, and smoking and its relationship to cancer incidence by various sites. Similarly in cancer screening and detection, quantified objectives related to the early diagnosis of specific cancers, taking into account effective screening technologies, are formulated. Treatment-related quantified objectives for morbidity and survival by cancer site or groups of sites are also presented. In cancer control surveillance recommendations for information feedback and evaluation of the cancer control plan, methods for identifying regions of the country where improvement in cancer control is possible or has been made, and, in general, recommendations on ways to track progress toward meeting cancer control objectives are considered.

In addition to formulating objectives, Federal, State, and community actions, programs and initiatives geared toward meeting the objectives are identified.

CANCER CONTROL SURVEILLANCE

Currently under development is a Surveillance Plan for the National Cancer Institute with emphasis on programmatic activities for the Division of Cancer Prevention and Control. This Surveillance Plan should play an important role in the coordination of surveillance activities as well as resulting in the efficient allocation of resources available for surveillance in monitoring progress towards the Year 2000 goals and objectives. In structuring the Plan, the following areas of surveillance activities have been identified: cancer mortality, cancer incidence, cancer patient survival, geographic hot spots of cancer, treatment, rehabilitation, risk factors, screening, ecological factors, economics, and cancer control program tracking. A summary of current and planned activities in each area of surveillance is being developed as well as the identification of special studies that are related to surveillance. This information will then serve as the basis for the development of a Surveillance Plan which should identify areas requiring additional priority and justification for these new initiatives; the report will be an important guide in development of surveillance projects.

Areas that have been identified as lacking in the availability of useful data for surveillance purposes are multiple cancer risk factors and screening. To rectify this, a Cancer Control Supplement to the 1987 National Health Interview Survey (NHIS), carried out by the National Center for Health Statistics (NCHS), is being developed in collaboration with the various program areas of the Division and, in particular, the Cancer Control Science Program. The survey will be based on a random sample of the total U.S. population which will include 52,000 adult respondents. The collected data will provide benchmark information on knowledge, attitudes, and practices related to cancer risk factors and screening in a number of population subgroups of interest. It is anticipated that this project will be the initial phase in establishing standardized procedures for monitoring knowledge, attitudes, and practices in the general population which are relevant to cancer control.

PROGRAM EVALUATION

The past year saw continuation of major program evaluation efforts-evaluation of the Community Clinical Oncology Program (CCOP) in cooperation with the Centers and Community Oncology Program, analytic support for the Year 2000 goal-setting process which is discussed under the Year 2000 goal modeling, and development of a plan for evaluation of the Physician Data Query (PDQ) project. The Community Cancer Care Evaluation project is studying three programs (the Cooperative Group Outreach Program, the Community Hospital Oncology Program, and the Community Clinical Oncology Program) to determine their level of success, independently and in collaboration with one another, in effectiving change in cancer care in the community setting.

PDQ-Evaluation

PDQ is a new computer-based information system aimed at providing physicians with the latest information on cancer treatment. This system was designed by NCI, and is available to physicians through the National Library of Medicine or through private vendors. It can be accessed on any home or office computer equipped with a modem. The PDQ system is part of the National Cancer Institute's efforts to provide, as efficiently and expediously as possible, the latest cancer treatment information to the practicing community. PDQ offers information on state-of-the-art and investigational cancer treatments, a listing of active cancer clinical trials, the patient eligibility requirements for entrance into those trials, and the investigators and contact persons associated with the trials. The system also contains a listing of cancer specialists, primarily members of appropriate specialty societies. Each of these files is cross-referenced by cancer site, geographic area, and medical subspecialty. An objective of the availability of PDQ is improved access to state-of-the-art cancer care, and ultimately, by acting in conjunction with other NCI community programs, improved cancer patient outcomes.

In order to determine the usefulness and impact of this system the SORB, in cooperation with the Health Promotion Sciences Branch, Cancer Control Science Program, is developing an evaluation strategy. The evaluation consists of four components: assessment of the process used to update and maintain the information within PDQ; assessment of the vendor implementations of the PDQ system; determination of user characteristics and reactions to PDQ, including perceived benefits and costs; and, finally, the impact of PDQ on practice and ultimately cancer mortality and/or morbidity.

An Evaluation Steering Committee has been established to guide activities of both NCI staff and contract staff funded to conduct the second and third components. This committee includes experts from the various disciplines related to the PDQ system including communications and information systems, technology transfer and diffusion, computer systems, and, of course, evaluation methods.

DATA MANAGEMENT AND IMPLEMENTATION OF LARGE-SCALE INTERVENTION TRIALS (Z01 CN 00109-03 SORB)

Research on these topics is prompted by the fact that large-scale, long-term controlled trials will be conducted by the DCPC Prevention and Cancer Control Science Programs during the next decade. Several activities important for the design, data management, and implementation of the current intramural trials in skin cancer and lung cancer prevention, in addition to broader research in controlled trials methodology, have been undertaken during this fiscal year. These activities are conducted by SORB staff within the Office of the Chief, the Operations Research Section, and the Computer Systems Section in collaboration with DCPC intramural staff in the Biometry Branch and the Cancer Prevention Studies Branch.

Data Coordinating Center

The Surveillance and Operations Research Branch is acting as the Data Coordinating Center for the "Use of Isotretinoin in Prevention of Basal Cell Carcinoma" Chemoprevention trial (Z01 CN 00103-03 CPSB). Data management and coordination responsibilities include:

- Randomization of study subjects to intervention groups;
- Design and development of data collection forms;
- Production of a detailed manual of procedures and operations;
- Preparation and administration of a training program for both the study coordinators and the principal investigators;
- Centralized data acquisition, processing, and management including quality assurance aspects of data and study endpoint determination;
- Monitoring systems for drug flow;
- Timely reporting and documentation of study data including reporting to the Data, Safety, and Monitoring Committee;
- Collaboration in the interim and final analyses of study data.

In FY 85 major revisions to the data collection procedures were made in order to streamline the system and focus on essential information without compromising quality control and monitoring for adverse reactions. Contracts to three new clinical centers with university affiliations were awarded in late FY 85; these clinical centers will randomized subjects into the trial to augment accrual from five existing military clinical facilities.

Pilot Studies for Intervention Trials

Pilot studies are a major component of large intervention trials, since the feasibility of many aspects of the large trial must be tested in a small scale study before launching into a project with anywhere from 2,000 to 20,000 patients. A pilot study for the "U.S.- Finland Beta-carotene, Alpha-tocopherol Lung Cancer Prevention Trial," (Z01 CN 00100-03 CPSB) completed in FY 85 demonstrates some of these parameters. This pilot study was conducted in one clinic over an eight month period. Objectives of the pilot were to: (1) evaluate utility of three different recruitment methods; (2) evaluate clinic operations procedures and on-site study administration logistics, including collecting and processing biological samples; (3) determine accuracy of smoking information on potential subjects; (4) assess short term compliance, and (5) monitor short term toxicity and its effect on the study "blind".

Of the 601 subjects invited to participate in the pilot trial, 39% were randomized, 32% were ineligible because of incorrect smoking status, 9% were ineligible for other reasons, 15% refused to participate, and 9% could not be contacted. Compliance, as assessed by pill count, was good. Due to the lower participation rate than had been anticipated, the age limit was extended to 50 years and a sixth clinic was added. The unreliability of smoking information has led to a pre-trial postal survey to establish this information prior to the initial clinic visit.

DESIGN, ANALYSIS, AND REPORTING OF RESEARCH STUDIES

Studies of Cancer Patient Survival (Z01 CN 00111-02 SORB)

A prospective population-based study of black/white differences in patient survival is being carried out in collaboration with the Health Promotion Sciences Branch for cancers of the breast, colon, corpus, and bladder. The purpose of the study is to identify prognostic factors of a behaviorial nature that are explanatory for black/white survival differences. Factors to be studied include nutrition, delay in seeking diagnosis, coping mechanisims, and access to medical care in conjunction with clinical and pathological characteristics of the disease and its treatment. Current plans call for accessing a total of 2,600 patients (1,300 blacks and 1,300 whites) for the four sites being studied. Patients who meet the eligibility criteria and who are diagnosed during the period January 1, 1985 through December 31, 1986 in three geographic areas of the country will be included in the study.

Pain Control in Cancer Patients

Analysis of data from a multi-institutional prospective study funded in 1979-1982 by the Community Oncology and Rehabilitation Branch (CORB), Centers and Community Oncology Program, has been in progress during the past year. Quality of the data base, inherited from the data management contractor, was carefully assessed with regard to completeness of critical data items and comparability across patients within and between the seven clinical sites. Documentation of the status of the data base and preliminary analyses of study results were produced. Activity continues to provide a final analysis and report for publication.

PLANS

Future activities will center on development of the National Cancer Institute Surveillance Plan, as well as a corresponding implementation plan. Continued leadership of the NCHS - NCI Coordinating Committee, with emphasis on the NHANES - III survey will occur. Analysis and reporting of results from the Community Cancer Care Evaluation project will be completed. Ongoing projects related to data management of large-scale intervention trials, and the design, analysis, and reporting of research studies will continue.

OPERATIONS RESEARCH SECTION

OBJECTIVES

The need for centralized analytic activities related to operations research applications in cancer control, especially resource allocation and statistical consultation, lead to creation of a new Section within the SORB. The Operations Research Section (ORS):

- Develops methods for and assists in the planning and management of cancer control resources, using operations research, epidemiological, statistical, and econometric techniques, as appropriate;
- plans and conducts studies which assist program managers in establishing program priorities and allocating cancer control resources to appropriate research and application activities;
- plans and conducts studies on the economics of cancer and on the economics of the three major types of cancer control activities, prevention, screening, and patient management;
- plans, conducts, and provides collaborative support for research and developmental activities which are related to monitoring progress toward cancer control in the United States; and
- conducts studies on evaluation methodology and provides analytic support for program evaluation activities in the Division.

CANCER CONTROL MODELING

An extensive collaboration has evolved during the year in developing analysis tools for modeling prevention, screening, and treatment program impact on incidence and mortality for the Year 2000 goals and objectives (Z01 CN 00142-01 SORB). This collaboration had included staff from both the Surveillance and Operations Research Branch and the Biometry Branch, as well as outside collaboration from Dr. David Eddy of Duke University.

During the year, the NCI staff (principally Dr. Levin of the Biometry Branch) has developed and written a large Fortran program for the NIH DEC-10 computer which is used to project cancer mortality and incidence figures from 1980 through the year 2000. The computer model is based partially on early work by Dr. David Eddy. The method incorporates different statistical models for survival from cancer, includes data for 40 separate cancer sites, includes the ability to examine temporal trends in underlying cancer incidence and in mortality from other causes, allows adjustment to 1970 or 1980 U.S. population standards, and produces projections of annual incidence and mortality statistics. The project has received considerable assistance from the Demographic Analysis Section staff with the provision of virtually all the input data.

This model has been used to estimate the impact of specific cancer control objectives on mortality in the Year 2000. The advantage of this modeling approach is that it provides a unified method for examining the contributions of prevention, screening, and treatment programs, with corresponding attention to comprehensiveness of program design and elucidation of tradeoffs in specific program decisions. Further efforts are ongoing in refinement of the methodologies used and in analyzing the output of the projections of cancer rates.

An expanded microcomputer version of the model developed by Dr. Eddy, which will be valuable as a planning tool for state and local agencies is under development. Crucial collaboration has been received from both the Demographic Analysis Section and the Cancer Control Applications Branch. This version of the model will be transportable to several microcomputer environments. In addition to simple projections of incidence and mortality rates, cost and quality of life factors are available to users. A detailed users manual is being drawn up with the intention of making the model available to state and local agencies in the near future.

ANALYSIS AND EVALUATION

Multiple Primary Cancers

Several major analytic activities have been undertaken during the past year or continued from earlier years (Z01 CN 00141-01 SORB). A study of multiple primary cancers using the entire SEER data base has been in the analysis phase and is nearing completion. This study will document repeat cancer patterns and allow hypothesis development concerning certain etiologic factors and the association of tumors. Such hypotheses have direct relevance for cancer control programs. For example, patterns of occurrence of multiple primaries in sites where dietary factors have been implicated as risk factors should provide additional insight into the frequency of occurrence of dietary related illnesses and the plausibility of the dietary hypotheses. High relative risks of developing a second primary for a type of cancer not thought to be linked to diet may suggest the need for additional epidemiologic study.

Prevalence of Cancer

Using the long historical data base of the Connecticut Tumor Registry, estimates of the prevalence of cancer are being generated. There are two separate focuses of this effort. First, developing these estimates will inform the Centers and Community Oncology Program (CCOP) concerning the baseline number of patients who are candidates for ongoing treatment protocols or potentially in need of rehabilitative care. This will aid the CCOP in designing cancer survivor surveys to help address the high priority needs of patients and families of cancer survivors. In addition, age-sex specific prevalence estimates by site are important epidemiologic indicators of chronic disease which have not appeared in the literature; the NCI should produce these because of their scientific contribution. Estimates from the entire SEER data base will be generated for cancer sites where the Connecticut data indicate that the availability of only twelve years of data will give a good estimate of prevalence.

NHANES-II Multiple Risk Factors

Another example of new analytic efforts is the collaboration on the Second Health and Nutrition Examination Survey (NHANES-II). A group of investigators have used NHANES-II data to create a profile of all major cancer risk factors, including smoking, diet, occupation, and anthropometric measurements (obesity). Investigators represent the SORB, the Cancer Prevention Studies Branch, the Diet and Cancer Branch, the Smoking, Tobacco and Cancer Program, the Cancer Control Applications Branch, and the DCPC biomedical computing support contractor, IMS, Inc. The major goal of the study is examination of risk factors that occur together in specific patterns in the U.S. population. This will be informative both from an epidemiologic standpoint and also from a programmatic perspective, where efficient program design might be aided by an understanding of these combinations of risk factors. In addition to the analysis of multiple risk factors the group will examine the major risk factors by themselves as appropriate. In preparation from the data base are separate studies of dietary fiber in the U.S., studies of the relationship of smoking to specific risk factors, examination of the distribution of occupational risk using indices developed by the National Institute of Safety and Health matched to the NHANES codes, and correlation of cancer mortality rates to NHANES risk data at the county level. Within the near future, a documented data base which may be used by other disease-oriented investigators, especially those engaged in heart disease research, will be made available.

Absent in the NHANES-II data base is information on knowledge, attitudes, and practices related to cancer risk factors and screening. Future analyses utilizing the proposed NHIS Cancer Control Supplement survey data should rectify this deficit and provide a more complete description of population subgroups amenable to effective cancer control interventions.

Psychological Aspects of Breast Cancer

Statistical and analytic collaboration with investigators from the Psychological Aspects of Breast Cancer (PABC) Study has been undertaken in the last year. This has consisted of working with Dr. Joan Bloom, under an IPA agreement and assigned to the Health Promotion Sciences Branch during FY 85, and David Pee of IMS, Inc. on several analyses of the data base. A paper on the development of a brief self-report measure of psychological functioning has been prepared. This paper describes the analysis, developing the risk measure, and examining changes in the measure over time for breast cancer patients compared to negative-biopsy and other surgical controls. Additional analyses using stochastic models for examining changes over time have been developed using this data base and are under study.

DIETARY ASSESSMENT RESEARCH

In progress are a number of methodologic studies of dietary assessment (Z01 CN 00110-03 SORB) to evaluate and improve the reliability and validity of dietary assessment. These include those described in the following sections.

Health Habits and History Questionnaire

In an effort to enhance the comparability between trials conducted by the Division and ensure the collection of data on important variables in a standard manner, a questionnaire, the Health Habits and History Questionnaire, was developed. For the dietary component, both the list of foods and the associated nutrient values were developed in a data-based approach, using the NHANES II dietary intake data on a representative sample of approximately 12,000 individuals.

The questionnaire was pretested, piloted with basal-cell carcinoma trial patients (Z01 CN 00103-03 CPSB), and reviewed by a panel of experts. The modified questionnaire was then examined for its ability to produce results similar to those of a diet diary, with respect to vitamins A and C, total calories, fat and percent of calories from fat. This provided a favorable evaluation of the adequacy of the food list, the precision of median nutrient values, and the utility of a small-medium-large approach to portion sizes. Work is in progress to evaluate the effect of eliminating items from the questionnaire and to develop regression models to predict the full questionnaire values to allow field trials of shorter versions of the questionnaire.

Validation Studies

Several field validations are planned or underway, in collaboration or cooperation with investigators at other institutions, using a variety of different populations and different reference methods. These include comparison with a diet history interview in a population with colon polys; comparison with several-day food records in a well population at high risk for skin cancer; comparison with multiple 24-hour recalls in an ill cancer patient population; comparison with objective evidence of food use in a normal Southwest population and in a population participating in a controlled feeding study on high and low fat diets. A reliability study is also in progress to assess the reproducibility of the instrument when administered in different seasons as compared to administration during the same season. Those studies which have been completed show good validity for a variety of macro- and micronutrients. In addition, the questionnaire assessment of vitamin supplement usage will be validated against detailed product information obtained from the actual supplement bottles brought to a clinic interview.

Data Management and Dietary Analysis

A complete data management system, including updating, range edits and dietary analysis, has been developed to accompany the Health Habits and History Questionnaire. Coding and analysis are rapid and inexpensive. An interactive personal computer system for administering and editing the questionnaire has been developed. Testing and evaluation of this system will be undertaken.

Retrospective Dietary Assessment

This project is assessing the validity of information about an individual's past dietary intake. The study makes use of subjects who provided multiple seven-day records seven to fifteen years ago. Their ability to provide information about their diet during that time period is being evaluated using both an interview and a self-administered questionnaire.

U.S.-Finland Dietary Assessment Validation and Reliability Studies

The U.S.-Finland Beta-Carotene, Alpha-Tocopherol Lung Cancer Prevention Trial (Z01 CN 00100-03 CPSB) will monitor dietary intake of these and other potentially important nutrients in over 17,000 high-risk men over several years. Two self-administered dietary survey instruments have been developed; one an extensive dietary history questionnaire with a color picture booklet for portion sizes, and the other a brief frequency questionnaire to monitor changes in diet. Reliability and validity studies have been carried out on both these instruments. For the validity studies, the reference method is the average intake from 12 two-day diet records collected over a six month period, in 200 men. The two reliability studies consist of three administrations of each instrument (each instrument in a different study group), conducted over different seasons. These studies provide support for the validity and adequacy of the dietary instruments used in this large lung cancer prevention trial. Analysis is in progress and papers are being prepared for publication.

Impact of Improved Precision of Carotenoid Analysis on Estimated Risk Levels in Epidemiologic Studies

The Diet and Cancer Branch will support the analysis of various retinoids and carotenoids in the U.S. food supply, in order to improve the data base on these components and permit the examination of their separate effects on cancer incidence. The Surveillance and Operations Research Branch, in collaboration with the Division of Cancer Etiology, will compare the results of case-control studies using the standard information on total carotenoids with the results using the newer HPLC information on specific carotenoids.

Consumption of Foods and Supplements Potentially Related to Cancer (Z01 CN 00111-03 SORB)

An estimated 30 percent of all cancers may be related to diet. The National Health and Nutrition Examination Survey (NHANES I and NHANES II) provide dietary data on a large representative national sample. Extensive organization and recoding of these data have resulted in a readily accessible data base permitting the analyses described below.

° Nutrient Sources in the U.S. Diet

This project provides a quantitation of the contribution of specific foods to energy and each of 18 nutrients including fiber. Two papers have been published this year from this analysis. For methodologic uses, this permits the identification of foods which could be omitted because of the infrequency of their consumption. For cancer control, this approach permits the identification of foods which may be appropriate targets of societal intervention, and provides persuasive data for policy makers or the public. It demonstrates, for example, that beef is the largest single contributor of fat in the U.S. diet, providing 18-20 percent of total saturated fat.

° Sources of Cancer-Associated Nutrients (Vitamins A, C and Fat) in Different Population Subgroups

This project has identified and quantified the sources of these nutrients in demographic or geographic subgroups. A paper on vitamin C by sex, race, and age group is in preparation. A paper on vitamin A indicator foods for various subgroups has been completed and is in press. This project will provide information with which to improve dietary assessment in subgroups, and may shed light on demographic differences in cancer incidence.

° Population Consumption of "Protective" or "Harmful" Foods

While the public is becoming increasingly aware of what constitutes a healthful diet with respect to cancer, there is less awareness of the extent to which actual eating habits conform to those recommended. The NHANES II data are being used to estimate the proportion of Americans consuming foods such as dark green leafy and deep yellow vegetables, fruits and vegetables rich in vitamins A and C, cereals high in fiber, red meat, fish, and fowl. Statistical analyses are in progress by race, sex, broad age groups, and poverty index, as permitted by the data. The project will provide information which may be useful in dietary interventions and public information campaigns.

° Demographic and Behavioral Correlates of Vitamin Supplement Usage

Patterns of vitamin supplement usage are being analyzed by demographic and behavioral characteristics, in a large representative national sample. Preliminary analyses have demonstrated, for example, a strong sex difference in supplement usage after control for other factors such as age and education. Such information may assist in the understanding of demographic differences in cancer incidence or survival.

PLANS

As indicated in the detailed description of the Year 2000 cancer control modeling project, additional efforts are needed in several specific areas. The first is a series of necessary refinements to the current model. One of the most crucial is reprogramming and examination of the competing risk problem in the case of changes in major competing causes of death, such as decline in cardiovascular disease mortality rates, and in the presence of hypothetical cancer control programs that will likely affect specific diseases in addition to the target cancer.

An additional extension is development of a uniform data base in the cost and quality of life area which can extend the use of the modeling to considering resource allocation problems. A new thrust of ORS activities will be consideration of resource allocation strategies in cancer control program planning. Using the cancer control model as a framework, we will examine available choices in cancer control, in prevention, screening, treatment, and rehabilitation with regard to resource allocation. This effort will work in concert with the emergence of additional efforts spent in research concerning the economics of cancer control. Specific issues to be addressed may include personal health expenditures and cancer prevention and early detection activities, insurance benefit structure and cancer control, and manpower and facility distribution for cancer related care.

ORS staff will continue to be involved in the development of the National Cancer Institute Surveillance Plan and in specific components of surveillance activities coordinated by other SORB staff. Specifically, contributions to selecting the study design and methods for dietary assessment to be used in the NCI Cancer Control Supplement to the National Center for Health Statistics' 1987 Health Interview Survey (HIS) have been made. Further methodological and substantive efforts are needed to help complete the instruments for this major surveillance project. Other surveillance efforts will continue to develop and will require the collaboration of ORS staff.

Several projects described earlier, including analysis of the NHANES-II data, the cancer prevalence study, and the multiple primary study will continue and are expected to have spinoffs related to their major aims during the year.

Future plans for dietary assessment methodology include expanding the diet questionnaire data base to permit calculations of nutrient estimates for vitamin E, folate, nitrates, and other factors. Development of an abbreviated diet questionnaire and accompanying regression model to permit accurate nutrient estimation with shorter instruments is in progress. Quantification of the NHANES I Follow-on Epidemiologic Study frequency questionnaire will be developed to permit substantive epidemiologic analyses of nutrient intakes and health outcomes. Lastly, future analytic activity includes description of population intake and sources of fiber, folate, and other nutrients.

DEMOGRAPHIC ANALYSIS SECTION

OBJECTIVES

An essential component to a wide variety of cancer prevention and control activities is the functional unit that coordinates a number of geographically-based cancer reporting systems which collect and maintain central cancer incidence data bases, and provides routine and special reports and analyses from the data bases relevant to cancer control activities.

Responsibilities of this Section reflect an expansion of previous activities and are summarized in its functional statements. The Demographic Analysis Section:

- Measures the impact of cancer on populations;
- determines cancer incidence and mortality rates; factors associated with rates above or below average; the association of demographic factors with the survival and morbidity of patients and the development of related methodology and statistical theory; and
- develops, coordinates, and evaluates data acquisition and data processing procedures of organizations participating in the SEER Program (Surveillance, Epidemiology, and End Results), including such aspects as quality control of case findings, data abstracting and coding.

CONDUCT OF SEER PROGRAM

The Demographic Analysis Section is responsible for the planning, development, conduct and analysis of program investigations concerning the incidence of and mortality (and hence patient survival) from cancer in various population subgroups. The primary task of the Section is the collection, evaluation and analysis of data from the Surveillance, Epidemiology and End Results (SEER) Program to determine factors associated with variation in rates, associations of cancer risks with demographic factors, and the development of related methodology and statistical theory. The section has responsibility for the evaluation of data gathering and processing procedures of the SEER Program as well as for quality control of case finding, data abstracting and coding.

Surveillance, Epidemiology and End Results (SEER) Program (Z01 CN 00118-13 SORB)

The SEER Program began in 1972 as an outgrowth of two earlier NCI programs, namely the End Results Program and the National Cancer Surveys. The original eight participants in the Program, i.e. Connecticut, Iowa, Detroit, New Mexico, Utah, and San Francisco, began collecting data for cases diagnosed in 1973; two others, Seattle and Atlanta, began coverage for 1974 and 1975 diagnoses, respectively. Metropolitan New Orleans, which began coverage for the SEER Program in 1974, is no longer a participant. In 1983, the State of New Jersey became a SEER participant. The SEER Program covers approximately 12% of the U.S. population.

The SEER Program functions through contracts in each area with local non-profit medically-oriented organizations. Each participant has its own abstract form to record data for all cancer patients seen in every hospital or other medical facility within the covered area. In addition, an attempt is made to obtain abstracted records for all residents diagnosed or treated for cancer outside the geographic area of coverage. All death certificates which mention cancer for residents of the area covered are abstracted regardless of the place of death. Additional information is requested from the physician signing the death certificate. Death certificates for all patients listed in the data base who have died are also abstracted to provide followup data to ensure complete coverage. The records of private pathology laboratories and radiotherapy units are also used to identify additional cases.

SEER Quality Control

Quality control aspects of the SEER Program are coordinated by a senior DAS staff member who plans, conducts, evaluates, and reports results of activities implemented by NCI staff and three individuals funded through a contract with the University of California. The SEER quality control program involves four major activities: field monitoring and special studies, conduct of workshops and seminars, development of training materials and manuals, and liaison with relevant professional organizations.

The six field staff routinely monitor each SEER contractor through case-finding audits to assure completeness of the incidence data. The SEER field representatives access source documents, independently searching out all cancer cases and compares their ascertainment with the registry list. Inconsistencies and omissions are investigated and resolved. The staff also implement procedures for reabstracting and recoding audits to evaluate accuracy and completeness of the reported information, again through access of source documents. Lastly, the field staff conduct special studies, such as review death certificate cases in patients under the age of 60 to determine their validity, review all cases with primary site unknown, review lymphomas and leukemias to determine if treatment-induced second primaries had been overlooked, review cases with multiple primaries in the same site to determine if they were true second primaries or metastatic disease, and field test new coding systems, such as extent of disease and treatment, to determine if the codes are logical and workable.

Unresolved question arising from quality control visits or from the registries, are entered into the SEER Inquiry System. Tentative answers are first reviewed by the SEER field representatives and than by all registries. Resolved answers are routinely distributed to the SEER participants; unresolved questions are then discussed at the semiannual SEER Workshops attended by abstractors and coders. These Workshops also include lectures on anatomy, treatment, diagnostic procedures, and extent of disease. Selected registries present reports on successful tumor registry methodology and SEER staff present reports on how registry data is being used. Individual workshops are conducted for registries with new personnel or with particular problems. Hospital registrars, especially those collecting data for the central registry, often attend. This training improves relationships between the hospital and the central registry, as well as improves data quality.

Development of training materials on case-finding methodology, abstracting guidelines, and exercises on determining extent of disease and staging of cancer are valuable adjuvant methods for quality control. The Self-Instructional Manuals for Tumor Registrars, used worldwide, provide a valuable source of training in the registry field. The SEER Program Manuals are also routinely updated. A staging manual that encompasses the SEER extent of disease, the American Joint Committee on Cancer (AJCC) staging system, and the historic staging of localized, regional, and distant disease is needed by hospitals across the country and is being developed. Numerous other relevant publications are developed and maintained. Lectures at annual professional meetings, and to state and regional tumor registry associations are often given.

Other quality control activities include liaison with non-SEER central registries, participation and leadership in the National Tumor Registrars Association, involvement with the American College of Surgeons, and evaluation of registry organization and practices. These activities promote a high level of tumor registry methodology at the hospital level throughout the nation.

During the past year quality control activities have concentrated on assuring completeness of case finding by the SEER contractors; hospitals over 300 bed size have been visited. Preliminary results indicate an improvement in completeness compared to 1979. However, these visits indicate more and more diagnoses are being made outside of the hospital setting as the result of DRGs. Thus, case finding methods may have to be revised to cover additional data sources in the future.

DATA BASE DEVELOPMENT

New Cancer Registries

Considerable effort has been expended in helping new and developing registries outside the SEER Program. This has been primarily in the area of on site staff training, but will expand to include quality control activities. The DAS, in cooperation with the Cancer Control Application Branch, has consulted extensively with individuals in geographic areas across the United States who are in the process of setting up population-based cancer reporting systems compatible with SEER reporting procedures. This collaboration has been in the form of staff training, providing SEER publications, supplying computer software, and critical evaluation of local manuals, materials and operating procedures.

SEER Processing

DAS staff coordinate central processing for creation of the SEER data base and analysis files. Data tapes received from the SEER registries in December of each year are generally through the edit-update procedures and ready for analysis by the following February. NCHS mortality tapes require additional processing to obtain population estimates or denominator data, used in calculation of cancer rates. Population estimates received from the Bureau of the Census lag two to three years behind the SEER cancer incidence and mortality data and therefore must be generated. Further, Census estimate do not contain sufficient race and ethnic detail to meet cancer surveillance needs and imputation procedures are executed to refine the official estimates and deduce the needed detail.

Year 2000 Databases for States

In collaboration with the Operations Research Section and the Cancer Control Applications Branch, a tool for cancer control planning and program development by states is being developed. Current mortality rates and numbers of deaths for each state and for each of the major cancer sites are being analyzed and extrapolated into the Year 2000. The national goals are then prorated by state and applied to each individual state's Year 2000 estimates. These estimates and expectations for the Year 2000 are being shared with the respective state's medical associations and state health departments in an attempt to involve more people in programs which relate to achievement of the Year 2000 goals.

ANALYTIC RESEARCH

Independently and in collaboration with other DCPC staff, DAS conducts a broad range of applied research and analytic activity in support of the Division mission.

Annual Cancer Statistics Review

Each year an updated statistical report on cancer incidence, mortality, and survival is produced from the SEER Program for the November meeting of the National Cancer Advisory Board. Data is given for all of the major cancer sites by race. Time trends in incidence, mortality, and survival are assessed in order to look for temporal changes by comparison with established trends to provide relevant cancer control surveillance information.

Survival and Trend Analyses

Breast cancer incidence, mortality, and survival have been analyzed by age and date of diagnosis to better understand the relationship between these three measures. An examination of differences by age was also undertaken for women with cancer of the ovary. Stage III-IV and unknown stage disease occurred more often with increasing age. Older women with Stage III-IV survived less well than younger women. In addition, there were remarkable changes in the type of treatment given over the period 1973-82. These results have prompted a similar extensive analysis of age, stage, and treatment for cancers of the breast, cervix uteri, and corpus uteri.

Socio-economic status (SES) differences may be able to explain observed differences in survival by different racial groups. Preliminary work has been started to evaluate which SES variables are important to delineate the true SES of an entire census tract. A preliminary study using the 1970 U.S. census tape and only four SEER areas showed that some of the black-white survival differences were lessened when SES was taken into account.

In an examination of tumors occurring before the age of 30 melanomas of the skin were among the five most common forms of cancer among both males and females between the age of 15-29. As in older adults, females develop melanomas on the extremities while males develop melanomas on the trunk.

AVAILABLE

Ewings' sarcomas occur in bones which run horizontally across the body while osteosarcomas develop in the long bones which run vertically. No explanation of this phenomena for tumors most prevalent during adolescence is known, but it does seem to relate to marrow production. Differences in the rates of childhood tumors between 1973-77 and 1978-82 are minimal. Major improvements in survival continue to be seen, particularly for Wilms' tumors and acute lymphocytic leukemias.

An analysis of the incidence of and survival from alcohol-related cancers indicated that blacks but not other minorities are at an increased risk. Japanese have an increased survival compared to whites while blacks and American Indians had considerably poorer survival. For cancers of the esophagus, liver, and pancreas all minorities, as well as whites, had extremely poor survival.

Recent case reports have suggested that the acquired immunodeficiency syndrome (AIDS) may be associated with cancers other than Kaposi's sarcomas. SEER data were used to examine these relationships by comparing the morbidity odds ratio (OR) for specific cancer sites in pre-and post-AIDS time periods. A significant increase was found for Burkitt-like lymphoma in San Francisco. These findings, not observed for other cancers in the remaining SEER registries, provide statistical support for the excess risk of Burkitt-like lymphoma in an age-sex group at risk of AIDS.

Disease Classification

The SEER Program has collected extent of disease information for each cancer site since 1973. This information, however, has varied in breadth and scope over time. The most recent major change was to simplify and condense the information into three fields: size of tumor, extension of tumor, and involvement of lymph nodes. These changes have required extensive re-writing of coding manuals and re-training of staff. These changes and inconsistencies between clinical and pathological sources of information have made it difficult to collapse data into meaningful staging categories. Despite problems, collapsing extent of disease information into American Joint Committee on Cancer (AJCC) stages is near completion. Progress is also being made in collapsing extent of disease into historical definitions of localized, regional, and distant categories for the major cancer sites.

The DAS coordinates an international death certificate study under auspices of the International Agency for Research on Cancer (IARC). The study has two parts. In Part I comparisons are made between coding 1000 death certificates using both ICD-9 and ICD-8 by each of nine participating countries. In Part II, each country submits 100 difficult-to-code death certificates which are then circulated and coded by all seven participating countries. Analysis and review of mismatches is used for making new recommendations to the World Health Organization for ICD-10. These two studies form the basis for development of additional coding rules which clarify disease classification rules for ICD-10.

ABLE

Other projects in progress investigate disease classification methodology and its relationship to interpretation of analytic results using diverse cancer data bases. An accuracy of death study for liver cancer has been initiated using SEER patients which involves comparison of hospital diagnosis with diagnosis on death certificates. Comparability ratios between ICD-8 and ICD-9 at the 3 digit and the 4 digit level are being developed for publication and subsequent use by researchers studying mortality trends. Other analysis activities include evaluating changes in SEER data by histologic types within sites, such as for Kaposi's sarcoma, angiosarcoma, and vaginal carcinoma. A study of persons having multiple cancers, one of which is a lypmphoma or leukemia, is also in progress.

INFORMATION DISSEMINATION AND PUBLICATIONS

The SEER data base is extensively used to respond to information requests from the scientific, medical, business, media, legal, government, and private sectors. The DAS is often consulted regarding proper uses of the SEER data and implications of analyses with respect to cancer control and prevention. Two illustrative examples are SEER data cited by Rose Kushner in a recent *CA* article, and a Chicago surgeon who learned through SEER data that their "epidemic" of lung cancer among black men was not unusual. Responses to requests for statistics for press releases, speeches by the NCI Director, and other inquiries were provided, often with short turn around deadlines.

Age-adjusted and age-specific cancer incidence and mortality rates for the individual years 1973-81, as well as for the composite years 1973-77 and 1978-81, were published for each county within the SEER geographic area. These rates updated those previously published for the years 1973-77 in *National Cancer Institute Monograph 57*. Incidence and mortality data for 1982 are now available, and data for 1983 will be available shortly.

In close collaboration with the Office of Cancer Communications, DAS staff co-edited the book *Cancer Rates and Risks*. DAS had primary responsibility for accuracy of all published statistics. Each year in cooperation with the NCI budget office DAS coordinates the tabular and graphic materials for the "Impact of the Disease" chapter in the *NCI Annual Plan and Fact Book*. Incidence and mortality data, both numbers and rates, are shared with the American Cancer Society (ACS) for use in their annual publication *Cancer Facts and Figures*, and in other publications.

INTERNATIONAL COLLABORATION

The DAS has participated at the international level with the World Health Organization, the International Agency for Research on Cancer, and the International Association of Cancer Registries, to promote standardized tumor nomenclature, reporting procedures, and definitions throughout the world. DAS staff serve on a WHO-IARC working committee to develop the neoplasm chapter of ICD-10 and revisions to the International Classification of Diseases for Oncology (ICD-O). New proposals for ICD-10 regarding cancer are tested utilizing the SEER data base and input from U.S. cancer registries is obtained through circulation of questionnaires on the proposals. A proposal for 4 digit subsite codes will be presented to the ICD-10 international meeting in December 1985. These activities are directly related to the continuity and accuracy of disease classification for the SEER data base. Collaboration with international scientists also occurs. Further, there has been direct collaboration with and financial support of the activities of the Israel Tumor Registry for the purpose of comparing trends in the incidence of and survival from cancer between Israel and the United States.

PLANS

During the coming year three comprehensive monographs are planned. One will detail for whites and eight specific minority groups incidence by primary site of cancer for the years 1978-82. There will also be a major section on cancer by histologic type in the white and black populations. A second monograph will be devoted to cancer mortality in SEER areas and the total United States for the same time period and covering the same racial-ethnic groups. The third monograph will deal with survival data for patients diagnosed in 1973-82 and will contain analysis by site, histology, extent of disease, sex, race, and treatment. Currently, all data are being summarized into the AJCC staging categories.

Plans will be developed to expand the coverage of the SEER Program to include another major Hispanic community. Also, ways to incorporate data from other U.S. population-based registries into the surveillance activities of the Section will be examined. Further, efforts will be made to find a mechanism to take advantage of data from hospital-based tumor registries to augment currently available survival data. Any effort to expand coverage will be accompanied by appropriate safeguards to insure quality control over additional data.

SEER data on multiple primary tumors will be presented at the International Association of Cancer Registries annual meeting. Staff will also prepare an exhibit of data and present results of specific research projects for the International Cancer Congress to be held in Budapest in August 1986. A visiting scientist from Osaka, Japan will spend six weeks with the staff to further investigate the survival advantage experienced by American Japanese compared to other U.S. minorities as well as the white population. Major emphasis will be placed on digestive cancers where the difference is most pronounced.

Efforts will continue with the AJCC to ensure that their staging categories actually delineate meaningful patient groups in terms of prognosis. The Breast Cancer Committee and the Committee for Liver, Gallbladder and Biliary Tract Cancers are currently using SEER data to revise staging schemes. Recommendations will be made both to the parent U.S. committee in January 1986 and to the international committees of the UICC in the spring of 1986.

Long term survival analysis can now be made on patients diagnosed in 1973-74 and 8-year and perhaps 10-year survival rates can be produced. A major effort will concentrate on restaging lung cancer patients diagnosed in the early years of the program since the coding schemes then in use are no longer compatible with AJCC staging criteria. Survival analyses comparing the Hispanic populations in New Mexico, San Francisco, and Puerto Rico will be undertaken.

LABLE

COMPUTER SYSTEMS SECTION

OBJECTIVES

Consolidation of computer systems development and support for the Division of Cancer Prevention and Control is provided by the reconstituted Computer Systems Section (CSS). The CSS:

- Provides comprehensive computer systems analysis, design, and programming support for Division research and administrative projects;
- designs and develops computer software systems for Division initiatives such as the SEER program;
- evaluates and develops state-of-the-art computer support approaches for cancer prevention and control projects;
- advises on data processing issues relative to Division extramural projects;
- provides computer training and guidance, consultation, and assistance to Division staff;
- selects, operates and maintains mainframe remote and microcomputer hardware and software systems in support of Division computer uses.

The SORB computer systems activities support both the scientific and the administrative data processing needs of the division. The support is provided through three mechanisms: (1) On-going consultation is provided regarding the automation aspects of many intramural and extramural projects. Most cancer control projects today involve use of computers, and hence a variety of questions must be addressed ranging from the need for a particular piece of computer hardware requested by one contractor to the relative economics of supporting a coordinating center through NIH facilities versus outside support. (2) General support activities include operation of a mainframe remote printing facility, acquisition and maintenance of microcomputer and terminal hardware, monitoring of computer accounts, and computer administrative reporting requirements. (3) Specific projects with a major data processing component are supported by systems analysis and programming activities. These specific projects are discussed below.

SEER SYSTEMS DEVELOPMENT AND PROCESSING

Comprehensive data processing support is provided to all aspects of the SEER Program (Z01 CN 00118-13 SORB). The semiannual submissions of the SEER regional registries are incorporated into a central data base, modifications and enhancements to the processing software are designed and developed, National Center for Health Statistics mortality tape data are added to the data base, general retrieval programs such as the Cancer Incidence and Surveillance System are developed and maintained, and routine and special analyses are generated. One significant enhancement to the SEER system added during the past year was a new edit system: In addition to improvements in the algorithms to detect invalid data, the routines were generalized to facilitate operation on the variety of systems used in the SEER regional registries. Distribution of these edit routines is expected to improved the quality and reliability of the SEER data used for monitoring the overall success of the national cancer program.

Systems and Programming Support

Many computer support activities consist of the design and programming of data retrievals and analyses for the research efforts described in more detail elsewhere in this report. For example, during the past year retrievals and analyses have been generated for the Biometry Branch's on-going project regarding Morbidity Among Long-Term Survivors of Childhood Cancer and Their Offspring (Z01 CN 00114-02 BB). Many other special analyses were generated from the SEER data base. A new effort regarding generating cancer prevalence estimates was started, and programming support for the modeling of cancer control intervention effects (Z01 CN 00142-01 SORB) was initiated.

Other systems analysis and programming support include assistance with the data management system for the Health Habits and History Questionnaire (Z01 CN 0110-03 SORB). Several efforts in cooperation with the Centers and Community Oncology Program, such as development of a patient log system for capturing and analyzing basic information regarding patients seen at the Community Clinical Oncology Program (CCOP) facilities are in progress.

With regard to administrative support, microcomputer data base systems for general projects, grants, and contracts monitoring and for the specific review of the Cancer Centers Program were introduced. These systems support the production of routine reports as well as special analyses and ad hoc inquiries. With experience the use of these systems is expected to grow, and similar support will be extended to all DCPC extramural programs.

The number of personal computers within the division expanded, and their use was also enhanced through the provision of training sessions. In addition to the data base systems described above, routine use concentrated on applying standard word-processing and electronic spreadsheet packages to DCPC problems. Other special uses included the cancer control modeling effort and a microcomputer implementation of the DCPC dietary questionnaire.

PLANS

Future plans include the continued enhancement of the programs described above as well as some new efforts: One just beginning is the incorporation of prevention information into NCI's PDQ data base. Computer support for this effort potentially will include a standalone module for direct use by the lay public as well as health care professionals. The in-house microcomputer use is being extended to include high-quality graphics to provide the visual impact needed for conveying the relevance of cancer control statistics. Finally, several new projects will be exploring use of distributed microcomputers to support chemoprevention trials and community programs.

SURVEILLANCE AND OPERATIONS RESEARCH BRANCH STAFF

Office of the Chief

Branch Chief	Edward J. Sondik, Ph.D.
Biostatistician	Brenda K. Edwards, Ph.D.
Mathematical Statistician	Benjamin F. Hankey, Sc.D.
Statistical Assistant	Josephine Davis
Secretary	Lillian Tauber

Operations Research Section

Section Head	Larry Kessler, Sc.D.
Staff Fellow	Gladys Block, Ph.D.
Health Statistician	Anne Baranovsky, M.S.
Health Statistician	Anne Hartman, M.S.
Epidemiology Trainee	Allen Feldman, M.D., M.P.H.
Secretary	Lisa Carter
Stay-In-School	Susana Martinez

Demographic Analysis Section

Section Head	John L. Young, Dr.P.H.
Statistician	John W. Horm, M.S.
Health Statistician	Ardyce Asire, M.S.
Health Statistician	Lynn G. Ries, M.S.
Health Statistician	Evelyn Shambaugh, M.A.
Survey Statistician	Constance Percy, M.S.
Medical Record Librarian	Betty Jean Cicero
Medical Record Librarian	Jack B. Cunningham
Medical Record Librarian	Mary Kruse
Statistical Assistant	Barbara Lyles
Secretary	Betty Davison
Clerk-Typist	Mary Krause

Computer Systems Section

Section Head	Thomas A. Marciniak, M.D.
Computer Specialist	Valerie Van Holten
Computer Systems Analyst	Mary Cusano
Computer Systems Anslyst	M. Darlene Naughton
Computer Systems Analyst	Vivian Pelham
Computer Systems Analyst	V. Calvin Hollingsworth
Computer Clerk	John Kelly
Editorial Assistant	Corinne Howley

Electrical Engineer (Summer Intern)	Elizabeth Carducci
Biomedical Engineer (Summer Intern)	Susan Day
Health Educator (Summer Intern)	Nancy Neef

SURVEILLANCE AND OPERATIONS RESEARCH BRANCH BIBLIOGRAPHY

Biggar, R. J., Horm, J. W., Lubin, J. H., Goedert, J. J., Greene, M. H., and Fraumeni, J. F., Jr.,: Changes in cancer risk in a population at risk of AIDS. JNCI 74: 793-797, 1985.

Block, G.: A review of validations of dietary assessment methods. Sourcebook on Cancer and Nutrition. First edition. IL, Chicago Marquis Professional Publications, 1985, pp. 70-82.

Block, G. and Hartman, A.: Understanding the results of epidemiologic studies. Sourcebook on Cancer and Nutrition. First edition. IL, Chicago Marquis Professional Publications, 1985, pp. 91-97.

Block, G., Dresser, C., Hartman, A., et. al.: Nutrient sources in the American diet, I: vitamins and minerals. American Journal of Epidemiology 122: 13-26, 1985.

Block, G., Dresser, C., Hartman, A., et. al.: Nutrient sources in the American diet II: macronutrients and fats. American Journal of Epidemiology 122: 27-40, 1985.

Borus, J. F., Olendzki, M. C., Kessler, L. G., Burns, B. J., Brandt, U. C., Broverman, C. A., and Henderson, P. A.: The 'offset' effect of mental health treatment on ambulatory medical care utilization and changes: month by month and grouped month analysis of a five-year study. Arch. of Gen. Psychiatry. 42: 573-580, 1985.

Cicero, J.: Legislation on health issues. The Abstract. 11 (2): 4-5, 1984.

Curtis, R. E., Kennedy, B. J., Myers, M. H., and Hankey, B. F.: Evaluation of AJC stomach cancer staging using the SEER population. Semin. Oncol. 12: 21-31, 1985.

Devesa, S. S., Horm, J. W., and Connelly, R. R.: Trends in lung cancer incidence and mortality in the United States (Chapter 3). In Mizell, M. and Correa, P. (Eds.): Lung Cancer: Causes and Prevention. Deerfield Beach, FL, Verlag Chemie International Inc., 1984, pp. 33-45.

Eaton, W. W., Holzer, C. E. III, Von Korff, M., Anthony, J. C, Helzer, J. E., George, L., Burnam, M. A., Boyd, J. H., Kessler, L. G., and Locke, B. Z. The design of the ECA Surveys: the control and measurement of error. Arch of Gen Psychiatry. 41: 942-948, 1984.

Eaton, W. W., and Kessler, L. G. (Eds.): Epidemiologic field methods in psychiatry: the NIMH epidemiologic catchment area program. Orlando, FL, Academic Press, 1985, 378 pp.

Edge, R. A., and Marciniak, T. A.: The ada environment. Proceedings of the Symposium on Computer Applications in Medical Care. pp. 882-885, 1984.

Edwards, B. K.: Overview, design issues in chemoprevention trials. In Sestili, M. A., (Ed.): Chemoprevention Clinical Trials, Problems and Solutions. NIH Publ. No. 85-2715, 1984, pp. 59-61.

Greenwald, P., Costlow, R., Prorok, P., and Sondik, E. J.: Screening in the context of cancer control. In Miller, A. B. (Ed.): Screening for Cancer. Orlando, FL, Academic Press, Inc., 1985, pp. 25-48.

Kessler, L. G., Amick, B. C., and Thompson, J.: Factors influencing the diagnosis of mental disorder among primary care patients. Med. Care. 23: 50-62, 1985.

Kessler, L. G., Cleary, P. C., and Burke, J. D.: Psychiatric disorders in primary care: results from a follow-up study. Arch of Gen Psychiatry. 42: 583-587, 1985.

Kouri, R. E., Levine, A. S., Edwards, B. K., McLemore, T. L., Vesell, E. S., and Nebert, D. W.: Source of interindividual variance in aryl hydrocarbon hydroxylase levels in mitogen-activated human lymphocytes. In Omenn, G., and Gelboin, H. (Eds.): Genetic Variability in Response to Chemical Exposure, Banbury Report 15. NY, Cold Spring Harber, Cold Spring Harbor Laboratory Press, 1984, pp. 131-144.

Levine, P., Steinhorn, S., Ries, L. G., and Aron, J.: Inflammatory breast cancer: the experience of the SEER program. JNCI 74: 291-298, 1985.

Marciniak, T. A.: An ada perspective. Proceedings of the Symposium on Computer Applications in Medical Care. pp. 875-877, 1984.

Marciniak, T. A.: Hospital microcomputing. Proceedings of the Symposium on Computer Applications in Medical Care. p. 204, 1984.

Page, H. S. and Asire, A. J. (Eds.): Cancer Rates and Risks, third edition. NIH Publ. No. 85-691, 1985, 136 pp.

Percy, C.: Alterations of cancer statistical data by the 8th and 9th revisions of the International Classification of Diseases (Chapter VI). In Hickey, R. C. and Clark, R. L. (Eds.): Current Problems in Cancer: Cancer Data Systems. IX (3): Chicago, IL, Year Book Medical Publishers, Inc., 1985, pp. 61-77.

Percy, C., Horm, J., and Goffman, T. E.: Trends in histologic types of lung cancer, SEER, 1973-1981, (Chapter 12). In Mizell, M. and Correa, P. (Eds.): Lung Cancer: Causes and Prevention. Deerfield Beach, FL, Verlag Chemie International Inc., 1984, pp. 153-159.

Posada, J. G. Jr., Marantz, A. B., Yeung, K. Y., Smith F. P., Delgado, G., Edwards, B. K., and Schein, P.S.: The cyclophosphamide, hexamethylmelamine, 5-fluorouracil (CHG) regimen in the treatment of advanced and recurrent ovarian cancer. Gynecol. Oncol. 20: 23-31, 1985.

Segaloff, A., Hankey, B. F., Carter, A. C., Escher, G. C., Ansfield, F. J., and Talley, R. W.: An evaluation of the effect of vincristine added to cyclophosphamide, 5-fluorouracil, methotrexate and prednisone in the treatment of advanced breast cancer. Breast Cancer Res. Treat. 5: 311-319, 1985.

Shambaugh, E. M.: Data sets, minimal and expanded. Proceedings of the General Session on Computers: Tenth Annual Meeting of the National Tumor Registrars Association. Computers and the Tumor Registry. 1985, pp. 19-30.

Shambaugh, E. M., Lum, D., and Akers, C.: Comparison of ACS and SEER site-specific surgical codes for cancer of the stomach. Field Liaison Newsletter: Commission on Cancer (special issue). 22-26, 1984.

Spencer, C. D., Weiss, R. B., Van Eys, J., Cohen, P., and Edwards, B.: Medulloblastoma metastatic to the marrow: report of four cases and review of the literature. J. of Neuro-Oncology. 2: 223-235, 1984.

Tager, A. M. and Sondik, E. J.: Economic evaluation of the benefits of cancer prevention and health promotion programs. MD Med. J. 34: 77-82, 1985.

Taube, C. A., Burns, B. J., and Kessler, L. G.: Patients of psychiatrists and psychologists in office based practice - 1980. American Psychologist. 39: 1435-1447, 1984.

Wesley, M. N. and Edwards, B. K.: Statistical considerations in the design, analysis and interpretation of clinical trials. Chapter 18 in, Diagnosis and Management of Breast Cancer. Marc E. Lippman, Editor. W.B. Saunders (In press)

Young, J. L., Jr. and Horm, J. W.: Cancer statistics in Maryland and the United States. MD Med. J. 34: 72-76, 1985.

Young, J. L., Jr., Ries, L. G., Pollack, E. S., Boss, L. P., and Baquet, C.: Cancer patient survival by racial/ethnic group: U.S., 1973-79. Morbidity and Mortality Weekly Report. 34 (18): HHS Publ. No. (CDC) 85-8017, 1985, pp. 248-250,255.

Young, J. L., Jr., Ries, L. G., Silverberg, E., Horm, J. W., and Miller, R. W.: Cancer Incidence, Survival and Mortality for Children Under 15 Years of Age: New York, American Cancer Society Professional Education Publication, 1985, 11 pp.

DCPC Intramural Project Inventory

Z01 CN 00100-03 CPSB	U.S.-Finland Studies of Nutrition and Cancer
Z01 CN 00101-03 CPSB	Human Studies of Diet and Nutrition
Z01 CN 00102-03 CPSB	Phase I Studies of Oral Synthetic Retinoids- 4 HPR
Z01 CN 00103-03 CPSB	Use of Isotretinoin in Prevention of Basal Cell Carcinoma
Z01 CN 00104-03 CPSB	NHANES I Epidemiologic Followup Survey: Chemoprevention/ Nutrition Aspects
Z01 CN 00105-03 BB	Research in Cancer Screening Methodology and Modeling
Z01 CN 00106-03 BB	Studies in Cancer Screening
Z01 CN 00107-03 BB	Design and Analysis of Pharmacokinetic Studies of Selenium
Z01 CN 00109-03 SORB	Data Management and Implementation of Large-Scale Intervention Trials
Z01 CN 00110-03 SORB	Methodologic Studies of Dietary Assessment
Z01 CN 00111-02 SORB	Consumption of Foods and Supplements Potentially Related to Cancer
Z01 CN 00112-02 CPSB	Nutrition Intervention Study in Esophageal Cancer in Linxian, China
Z01 CN 00113-02 BB	Cancer in Oriental Populations
Z01 CN 00114-02 BB	Morbidity Among Long-Term Survivors of Childhood Cancer and Their Offspring
Z01 CN 00115-02 BB	Descriptive Cancer Epidemiology
Z01 CN 00116-02 BB	Statistical Methodology Research
Z01 CN 00117-02 SORB	Black-White Differences in Cancer Patient Survival
Z01 CN 00118-13 SORB	Surveillance, Epidemiology, and End Results (SEER) Program
Z01 CN 00119-02 BB	Consultation on Clinical Trials and Other Studies
Z01 CN 00121-01 BB	Research in Biostatistical Methodology and Mathematical Modeling
Z01 CN 00122-01 BB	Development of Cancer Control Epidemiologic Methods
Z01 CN 00141-01 SORB	Modeling and Statistical Analysis Related to Cancer Control

Z01 CN 00142-01 SORB	Cancer Control Objectives and Cancer Mortality Projections
Z01 CN 00143-01 CPSB	Analysis from Long-Term Followup Data from the BCDDP Project
Z01 CN 00144-01 CPSB	Lung Cancer Intervention Study Among Yunnan Tin Miners-Feasibility Study

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00100-03 CPSB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
U.S.-Finland Studies of Nutrition and Cancer

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D.A. Albanes, M.D.	Staff Fellow	CPSB, DCPC, NCI
Others:	P.R. Taylor, M.D.	Act. Dep. Br. Chief	CPSB, DCPC, NCI
	B.K. Edwards, Ph.D.	Biostatistician	CPSB, DCPC, NCI
	A.M. Hartman, M.S.	Health Statistician	CPSB, DCPC, NCI

COOPERATING UNITS *(if any)*
National Public Health Institute, Helsinki, Finland
Surveillance and Operations Research Branch, DCPC

LAB/BRANCH
Cancer Prevention Studies Branch DCPC

SECTION

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	1.75	0.25

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The important relationship of diet and nutrition in the development of cancer has become well known through various research efforts. Laboratory studies have shown cancer inhibitory function for various natural and synthetic nutrients in various models, which have been corroborated by human epidemiologic studies of nutrient intake, tissue levels, and cancer incidence. Vitamin A, beta-carotene, and selenium have been strongly implicated for their cancer preventive potential, with sufficient evidence for these substances to warrant their use in prevention trials. In addition, the roles of other nutrients in cancer cause and prevention (e.g., dietary fats and fiber) require further investigation.

The objectives of this cooperative project with the government of Finland are: (1) to determine if either beta-carotene or alpha-tocopherol supplement is effective in preventing lung cancer in smokers, (2) to better assess the role of fats, selenium, and vitamins A, E, and C in breast cancer developement; and (3) to evaluate the relation of intake of various nutrients to subsequent cancer. The project includes three studies. The first is a 5-year, randomized, double-blind, placebo-controlled, 2x2 factorial prevention trial of daily beta-carotene (20 mg daily) and alpha-tocopherol (50 mg daily) among smokers at high risk for lung cancer. The difference in lung cancer incidence between intervention groups will be determined. The second is a breast cancer case-control study of fats, total calories, selenium, and vitamins A, E, and C. The role of various anthropometric measurements as well as genetic markers for breast cancer will be explored. The third project will be a comparison of nutrient intakes in cases and reference subjects identified from an existing large cohort with prediagnostic baseline dietary histories. Associations between various dietary components and several cancers will be assessed. Several pilot studies have been completed to date, and the prevention trial and breast cancer study are underway.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 CN 00101-03 CPSB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)
Human Studies of Diet and Nutrition

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

PI'S:	P.R. Taylor, M.D.	Act. Dep. Br. Chief	CPSB, DCPC, NCI
	D.Y. Jones, Ph.D.	Staff Fellow	CPSB, DCPC, NCI
	M.S. Micozzi, M.D., M.S.	Staff Fellow	CPSB, DCPC, NCI
	A.S. Schatzkin, M.D., Dr. P.H.	Staff Fellow	CPSB, DCPC, NCI
	Elaine Lanza, Ph.D.	Senior Investigator	DCB, DCPC, NCI
Others:	B.H. Patterson, M.S.	Math. Statistician	BB, DCPC, NCI
	B.K. Edwards, Ph.D.	Biostatistician	SORB, DCPC, NCI

COOPERATING UNITS (if any)
U.S. Department of Agriculture, Beltsville, Human Nutrition Research Center
Surveillance and Operations Research Branch, DCPC
Biometry Branch, DCPC

LAB/BRANCH
Cancer Prevention Studies Branch, DCPC

SECTION

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.0	2.25	0.75

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☒ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

The role of dietary factors in cancer prevention has been assessed in animal experiments, in human epidemiologic studies, and, most recently, in prevention trials. For many of these agents, however, information is incomplete concerning their safety, toxicity, dose, form, bioavailability, pharmacokinetics, and mechanism of action. To further define these parameters in humans, a cooperative research effort between the Beltsville Human Nutrition Research Center (BHNRC), U.S. Department of Agriculture, and the CPSB, DCPC, is being conducted. The overall goal of this collaborative effort is to obtain further information on potential cancer preventive agents. Initial efforts have focused on 3 nutrients which have shown the most promise for cancer prevention--selenium, fat, and beta-carotene.

A study of the kinetics of a single, oral dose of two forms of selenium in the fasting and non-fasting state was conducted in the first year. Future activities will evaluate the safety/toxicity of selenium and form of ingestion among persons residing in seleniferous areas.

Our first study of fat focused on potential mechanisms of action and will assist us in the evaluation of the relation of type and amount of dietary fat to hormonal status, bile acid metabolism, and fecal mutagenic active in premenopausal women. Subsequent evaluations will examine the relation of dietary fat and fiber to fecal mutagens in men, focusing on the prominent mutagen, fecapentaene.

Beta-carotene studies are examining the plasma carotenoid response to single and long-term ingestion of beta-carotene from either a capsule or from selected vegetables.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CN 00102-03 CPSB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Phase I Studies of Oral Synthetic Retinoids - 4 HPR

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	Earl Gross, M.D.,	Expert	CPSB, DCPC, NCI
Others:	J.A. Tangrea, M.P.H.	Pharm. Res. Coord.	CPSB, DCPC, NCI
	B.K. Edwards, Ph.D	Biostatistician	SORB, DCPC, NCI
	P.R. Taylor, M.D.	Act. Dep. Br. Chief	CPSB, DCPC, NCI

COOPERATING UNITS *(if any)*
Dermatology Branch, NCI
Surveillance and Operations Research Branch, DCPC

LAB/BRANCH
Cancer Prevention Studies Branch, DCPC

SECTION

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.9	0.1

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Phase I studies are needed to provide the parameters and characteristics of acute human toxicity, establish a maximally tolerated dose, delinate basic pharmacokinetics, and indicate a starting clinical dose for Phase III trials of the investigational drug.

Based on the *in vitro* and *in vivo* evidence that vitamin A and its synthetic analogs are active in the neoplasia process and case reports demonstrating the successful chemoprevention of basal cell carcinoma with large doses of the retinoid isotretinoin, a Phase I intramural clinical trial of a promising new oral synthetic retinoid, 4-HPR (N-4-[hydroxyphenyl]-retinamide), has been implemented. This study has the following objectives:

- Delineate acute human toxicity patterns of orally administered 4-HPR
- Determine a maximum tolerated/feasible dose (MT/FD)
- Evaluate the subacute toxicity of the MT/FD for 3 months
- Observe evidence of any therapeutic effect on specific cutaneous diseases and disorders of keratinization.

Five patients in good general health but with multiple basal cell carcinomas initiated therapy at 800 mg/day. Toxicity was observed within 3 weeks in 3 different patients and further testing was discontinued.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

ZN CN 00103-03 CPSB

PERIOD COVERED

October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Use of Isotretinoin in Prevention of Basal Cell Carcinoma

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	J.A. Tangrea, M.P.H.	Pharm. Res. Coord.	CPSB, DCPC, NCI
Others:	P.R. Taylor, M.D.	Act. Dep. Br. Chief	CPSB, DCPC, NCI
	B.K. Edwards, Ph.D.	Biostatistician	SORB, DCPC, NCI
	A.M. Hartman, M.S.	Health Statistician	SORB, DCPC, NCI

COOPERATING UNITS *(if any)* Walter Reed Army Medical Center, Fitzsimons Army Medical Center, Brooke Army Medical Center, Eisenhower Army Medical Center, Portsmouth Naval Medical Center, Dermatology Branch, NCI Radiology Department, Clinical Center, Surveillance and Operations Branch, DCPC

LAB/BRANCH

Cancer Prevention Studies Branch, DCPC

SECTION

INSTITUTE AND LOCATION

National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
4.0	3.25	0.75

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The study is a 5-year, randomized, double-blind clinical trial designed to evaluate the effectiveness of low dosage levels of isotretinoin in reducing the incidence of basal cell carcinoma in a high risk population, and to examine possible side effects associated with long-term administration of low doses of isotretinoin. Approximately 1,200 evaluable subjects will be entered into the study within 18 months at 8 participating clinical centers located around the country. At each center, subjects will be randomly allocated to intervention (10 mg/day) or control (placebo) groups.

The rationale for this study includes the following. Laboratory experiments have shown that retinoids administered to animals can prevent chemical carcinogenesis. In the experimental animals, retinoids were effective even if administered after exposure to the carcinogen, and therefore the prophylactic effect of the retinoids is believed to be in the post-initiation phase, i.e., during the promotion phase of carcinogenesis. Recent case reports have shown that isotretinoin can prevent the appearance of new basal cell carcinomas for four years in patients at higher risk of developing new tumors.

LABLE

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00104-03 CPSB

PERIOD COVERED

October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

NHANES I Epidemiologic Followup Survey: Chemoprevention/Nutrition Aspects

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI's:	P.R. Taylor, M.D.	Act. Dep. Br. Chief	CPSB, DCPC, NCI
	G. Block, Ph.D.	Staff Fellow	SORB, DCPC, NCI
	D.Y. Jones, Ph.D.	Staff Fellow	CPSB, DCPC, NCI

Others: This research is being developed as a collaborative effort by NCHS and various institutes at NIH.

COOPERATING UNITS *(if any)* Surveillance and Operations Research Branch, DCPC
Biometry Branch, DCPC
NCI, NIA, NIMH, NIAAA, NHLBI, NINCDS, NIADDK, NIAID
National Center for Health Statistics.

LAB/BRANCH

Cancer Prevention Studies Branch, DCPC

SECTION

INSTITUTE AND LOCATION

National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.75	0.75	0

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of the NHANES (National Health and Nutrition Examination Survey) Initial Epidemiologic Followup Survey was to conduct a longitudinal study of 14,407 adults originally surveyed in 1971-1975, to investigate subsequent health and mortality outcomes. Respondents have been traced and re-examined. Additional information was obtained from hosptial records, the National Death Index and death certificates. The NHANES Initial Followup Survey was completed in 1984.

The purpose of this intramural project is to examine the relationship of chemopreventive and nutritional factors as well as constitutional factors to cancer in this representive population. This study provides an opportunity to examine these factors and potentially confounding or modifying factors in a prospective fashion, and to examine the effectiveness of dietary agents which are currently of great interest for cancer prevention. The relationship of baseline vitamin use, biochemical or nutritional measures and subsequent health status will be examined. In addition, descriptive data and trends in potential risk factors or protective factors over time will be examined. A continued Followup, of the elderly (those over 75 years of age) started in 1985 while the entire cohort will be followed up in 1986.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00105-03 BB

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Research in Cancer Screening Methodology and Modeling

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	P. C. Prorok	Chief	SS, BB, DCPC, NCI
Others:	R. J. Connor	Mathematical Statistician	SS, BB, DCPC, NCI
	S. G. Baker	Staff Fellow	SS, BB, DCPC, NCI
	D. L. Weed	Senior Staff Fellow	BMCCES, BB, DCPC, NCI
	J. L. Aron	Senior Staff Fellow	EMS, BB, DCE, NCI

COOPERATING UNITS *(if any)*

LAB/BRANCH

Biometry Branch

SECTION

Screening Section

INSTITUTE AND LOCATION

NCI, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.1	.4

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☐ (a1) Minors

☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The focus of this project is development and refinement of statistical procedures for the design and analysis of cancer screening and related studies. Statistical problems under investigation include sample size determination, development and comparison of data analysis methods, and development of monitoring procedures for screening trials. Each of these problem areas is common to screening and prevention trials in which the Division participates, but the methods for screening studies must address the special lead time and length biases inherent in screening programs.

A procedure based on a statistical test for paired data has been developed to determine the sample size required when comparing the sensitivity of two screening tests in the situation where both tests are performed on a group of subjects and individuals positive on either test receive a diagnostic workup. Survival data of breast cancer cases in the HIP study were analyzed using competing risk theory to determine if screening produced delay or elimination of mortality. It was concluded that some breast cancer cases detected by screening realized a cure. 'Research into stopping procedures for screening trials uses cost-benefit methodology to determine whether to stop or continue a study. A Baysian approach for updating information at successive points in time is utilized. Models of disease and screening are being developed to aid in the interpretation and monitoring of colon cancer screening programs. Properties of case-control studies in the context of screening evaluation are also being considered. Alternative definitions of cases, controls, and exposure periods will be analyzed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00106-03 BB

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Studies in Cancer Screening

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	P. C. Prorok	Chief	SS, BB, DCPC, NCI
Others:	R. J. Connor	Mathematical Statistician	SS, BB, DCPC, NCI
	S. G. Baker	Staff Fellow	SS, BB, DCPC, NCI
	T. J. Mason	Chief	PSS, EEB, DCE, NCI
	J. Sobell	Epidemiologist	SS, BB, DCPC, NCI

COOPERATING UNITS *(if any)* DuPont Company (W. Neeld), Health Insurance Plan of Greater New York (W. Venet), International Agency for Research on Cancer (N. Day), National Institute for Occupational Safety and Health (R. Roscoe), International Union Against Cancer (A.B. Miller)

LAB/BRANCH

Biometry Branch

SECTION

Screening Section

INSTITUTE AND LOCATION

NCI, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.1	0.4

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

☒ (a1) Minors

☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Data from several cancer screening studies are being collected and analyzed to gain a better understanding of the impact and consequences of such screening in various population settings, and to develop new techniques for data analysis. Results from the Health Insurance Plan of New York breast cancer screening trial continue to indicate a reduction in breast cancer mortality. The long term follow-up phase of the study is nearing completion. A trial of the Hemoccult test for blood in the stool for the early detection of colorectal cancer is in progress.

The working group on cervical cancer screening of the IARC analyzed data from screening programs in Scandinavia, Scotland, Canada, and Italy on the incidence rates of cancer after negative screens. Results indicate that the maximum achievable reduction in risk is about 90 percent with annual screening starting at age 20. The screening evaluation project of the UICC concluded that screening for cervical cancer every three years provides practically the same benefit as annual screening and that the same screening frequency should be used irrespective of age.

Two occupational high risk groups are under scrutiny. In collaboration with DCE, the bladder cancer screening program at the DuPont Company is being analyzed to relate disease characteristics and outcome to urine cytology and blood tests, smoking history and chemical exposure. With DCE, and NIOSH updated follow-up data are being collected in a study of sputum cytology screening for lung cancer among uranium miners. The relationships among cytology classification, radiation exposure, smoking history, lung cancer, and mortality data will be analyzed.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00107-03 BB

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Design and Analysis of Pharmacokinetic Studies of Selenium

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI: B. Patterson	Mathematical Statistician	CDTS, BB, DCPC, NCI
Others: L. A. Zech	Senior Scientist	LTB, DCBC, NCI

COOPERATING UNITS *(if any)*

Cancer Prevention Studies Branch
Laboratory of Mathematical Biology, DCPC

LAB/BRANCH

Operations Research Branch, DCPC

SECTION

INSTITUTE AND LOCATION

National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
.4	0.5	0.1

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Selenium is a possible cancer preventive agent, and is being considered for use in intervention trials. A study in collaboration with the Cancer Prevention Studies Branch (Z01 CN 00101 CPSB) is in progress which will provide information on the pharmacokinetics of selenium in its prototype forms -- sodium selenite (inorganic form) and selenomethionine (organic form). This information is unavailable for these agents in the dose currently considered optimal, and is necessary to the determination of time and manner of administration. Parameters such as percent absorption, maximum concentration, time to maximum concentration and mean residence time will be estimated for a single dose and compared in fasting and non-tasting subjects.

In order to interpret the study data more fully, development of integrated kinetic models, one for selenite and one for selenomethionine, will be attempted. Such models are useful in making inferences about drug metabolism and about the distribution of the drug in various body pools. A model for selenite is under development. It is anticipated that the models will result in population estimates of mean residence times and rates of exchange between body pools.

The Biometry Branch, in cooperation with the Cancer Prevention Studies Branch, is functioning as a data collection center, had primary responsibility for the study design, and has primary responsibility for data analysis.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00109-03 SORB

PERIOD COVERED

October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Data Management and Implementation of Large-Scale Intervention Trials

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	Brenda K. Edwards, Ph.D.	Biostatistician	SORB, DCPC, NCI
Others:	Thomas A. Marciniak, M.D.	Medical Systems Analyst	SORB, DCPC, NCI
	Anne Hartman, M.S.	Health Statistician	SORB, DCPC, NCI
	Blossom Patterson, M.S.	Mathematical Statistician	SORB, DCPC, NCI
	Oscar M. Chavez	Statistical Assistant	SORB, DCPC, NCI

COOPERATING UNITS *(if any)*

Biometry Branch, DCPC
Cancer Prevention Studies Branch, DCPC
IMS, Inc. (biomedical computing support contractor)

LAB/BRANCH

Surveillance and Operations Research Branch, DCPC

SECTION

INSTITUTE AND LOCATION

National Cancer Institute, NIH, Bethesda, MD 20892-4200

TOTAL MAN-YEARS: 1.75	PROFESSIONAL: 1.50	OTHER: 0.25

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Several activities important for the design, data management, and implementation of the intramural controlled trials (Z01 CN 00103-03 CPSB and Z01 CN 00100-03 CPSB) have been undertaken during this fiscal year. In addition, broader research in controlled clinical trials has been conducted. Descriptions follow.

The Surveillance and Operations Research Branch functions as the Data Coordinating Center for the "Use of Isotretinoin in the Prevention of Basal Cell Carcinoma" chemoprevention trial (Z01 CN 00103-03 CPSB). Responsibilities include all of the usual ones for a data coordinating center as well as preparation and administration of a training program for both the clinical study coordinators and the principal investigators, and collaboration in the interim and final analyses of study data.

A model for training clinic personnel in on-site study administration and patient management was developed which assures standardized study operations according to protocol requirements and allows objective assessment of study coordinator skills. A prototype system using microcomputers for distributed data collection and limited processing was developed for a multi-institutional feasibility intervention trial among high risk occupational cohorts. The use of distributed microcomputers to support chemoprevention trials and community progress was initiated. Pilot studies are a major component of large intervention trials, since the feasibility of many parameters needs to be tested before launching into a study with 2,000 or 20,000 patients. The "U.S.-Finland Beta-carotene, Alpha-tocopherol/Lung Cancer Prevention Trial" pilot study, completed in FY 1984 in collaboration with the Prevention Program, demonstrates some of these parameters.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00110-03 SORB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Methodologic Studies of Dietary Assessment

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	G. Block, Ph.D.	Staff Fellow	SORB, DCPC, NCI
Others:	A. M. Hartman, M.S.	Health Statistician	SORB, DCPC, NCI
	J. Sobell, M.S.	Epidemiologist	BB, DCPC, NCI

COOPERATING UNITS *(if any)*
Cancer Prevention Studies Branch, DCPC; Biometry Branch, DCPC;
National Institute on Aging; National Center for Health Statistics

LAB/BRANCH
Surveillance and Operations Research Branch

SECTION
Operations Research Section

INSTITUTE AND LOCATION
National Cancer Institute, NIH Bethesda, MD 20892-4200

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.1	2.0	0.1

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A number of projects are in progress to evaluate and improve the reliability and validity of dietary assessment. A self-administered diet history questionnaire has been developed and piloted, and evaluations of the food list and quantitation methods indicate a high degree of agreement with a reference method. Field validation studies have been conducted in several different populations and using several different reference methods.

Efforts toward the improvement of nutrient estimation in quantified diet questionnaires have included the development of a nutrient data base and portion sizes based on data from 12,000 respondents in the National Health and Nutrition Examination Survey. A data management and diet analysis system for use with the self-administered diet history has been expanded and improved. An interactive computer system for administration and editing of the dietary questionnaire has been developed and will be tested.

In conjunction with the U.S.-Finland Beta-Carotene, Alpha-Tocopherol Lung Cancer Prevention Trial (Z01 CN 00100-03 CPSB), field studies to assess the validity and reliability of the extensive, self-administered instruments used in that trial have been completed. Analysis is in progress.

An evaluation of the accuracy of retrospective dietary assessment is being carried out, using subjects who provided multiple seven-day diet diaries seven to fifteen years ago. Their ability to provide information about their diet during that time period is being evaluated using both an interview and a self-administered questionnaire. In addition to the above dietary assessment methodology studies, an effort has been undertaken to evaluate the impact of improved carotenoid analysis on estimated risk levels in epidemiologic studies.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CN 00111-02 SORB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)
Consumption of Foods and Supplements Potentially Related to Cancer

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

PI:	G. Block, Ph.D.	Staff Fellow	SORB, DCPC, NCI
Others:	B. H. Patterson, M.S.	Mathematical Statistician	BB, DCPC, NCI
	A. M. Hartman, M.S.	Health Statistician	SORB, DCPC, NCI
	P. R. Taylor, M.D.	Acting Deputy Branch Chief	CPSB, DCPC, NCI

COOPERATING UNITS (if any)
Biometry Branch, DCPC
Cancer Prevention Studies Branch, DCPC
National Center for Health Statistics

LAB/BRANCH
Surveillance and Operations Research Branch, DCPC

SECTION
Operations Research Section

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, MD 20892-4200

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.1	1.0	0.1

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
  ☐ (a1) Minors
  ☐ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

Several projects are ongoing, designed to identify indicator foods for methodologic uses, and to describe the population's behavior with respect to potentially protective or harmful foods or nutritional supplements. Such efforts support the dietary assessments and monitoring necessary for cancer control, provide data on which to base population interventions or strategies, and shed light on factors which may influence observed subgroup differences in cancer incidence or survival.

Quantitative data on nutrient sources in the U.S. diet for energy and each of 17 nutrients have been developed resulting in two published papers. These data permit the identification of foods which make quantitatively important contributions to the population's intake of, for example, vitamin A or saturated fat. Similar analyses are under way for fiber and folate. A follow-on project has also provided this type of analysis for demographic or geographic subgroups. As part of this project a paper on vitamin A indicator foods for various subgroups has been completed and is in press. A paper on vitamin C is in preparation. Information from the whole project may aid in efforts to improve dietary assessment and dietary behavior in subgroups, as well as to understand possible reasons for observed differences in cancer incidence or survival.

An analysis of the proportion of Americans consuming potentially beneficial or harmful foods, such as high-fiber foods or red meat, is being carried out for each of several categories by race, sex, age and poverty status. The results may be useful in dietary interventions and public information campaigns. Demographic and behavioral correlates of vitamin supplement usage will be described using a large representative national sample.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CN 00112-02 CPSB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Nutrition Intervention Study in Esophageal Cancer in Linxian, China

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	P.R. Taylor, M.D.	Act. Dep. Br. Chief	CPSB, DCPC, NCI
Others:	J.A. Tangrea, M.P.H.	Pharm. Res. Coord.	CPSB, DCPC, NCI

COOPERATING UNITS *(if any)*
Cancer Institute, Chinese Academy of Medical Sciences, Beijing, The Peoples' Republic of China
Biostatistics Branch, DCE, NCI

LAB/BRANCH
Cancer Prevention Studies Branch, DCPC

SECTION

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to conduct two intervention trials using multiple vitami[illegible]mineral supplements to evaluate the relationship between such supplements and esophageal cancer incidence and mortality. One trial is being conducted in patients diagnosed with esophageal dysplasia (n = 3400) and the other in the general population in a high risk region (n = 30,000). The effect of these supplements on regression/progression of esophageal dysplasia and total cancer incidence, total cancer mortality, and total mortality will be evaluated. These two studies are being conducted in Linxian (Henan Province) in the Peoples' Republic of China (PRC). Linxian, a rural country with population 800,000 was selected because it has the highest rate of esophageal cancer in the world (>100/100,000) and because there is suspicion that the population's chronic deficiences of multiple nutrients may be etiologically involved.

This study is being conducted jointly by the Biostatistics Branch of the Division of Cancer Etiology and the Cancer Prevention Studies Branch of the Division of Cancer Prevention and Control at the NCI in collaboration with the Cancer Institute of the Chinese Academy of Medical Sciences.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00113-02 BB

PERIOD COVERED

October 1, 1984 - September 30, 1985

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)

Cancer in Oriental Populations

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

PI:	H. King	Research Sociologist	BB, DCPC, NCI
Others:	F. B. Locke	Statistician	BB, DCPC, NCI

COOPERATING UNITS (if any)

LAB/BRANCH

Biometry Branch, DCPC

SECTION

Biostatistical Methodology and Cancer Control Epidemiology Section

INSTITUTE AND LOCATION

National Cancer Institute, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	1.8	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

Studies of cancer among Chinese and Japanese in the U.S. and homeland counterparts are conducted to ascertain the transitional effect at geographical and generational (nativity) levels, and to elicit clues to the mapping out of cancer prevention and control programs for U.S. Orientals and other populations. The past limitation on U.S. Chinese studies was resolved by the release of the 1975 People's Republic of China (PRC) national mortality survey findings. Studies include:

- A study of cancer mortality among the Chinese in the U.S. (by nativity), Hong Kong, and Guangdong province in the PRC.
- A second project examines cancer mortality among Chinese in Singapore and the two provinces of Taiwan and Fujian.
- A third study ascertains health risks for Chinatowners in San Francisco and New York City, with particular reference to cancer control and prevention.
- A fourth study analyzes the incidence, mortality, and survival statistics on Chinese and Japanese groups in the SEER areas of San Francisco and Hawaii and incidence data on Los Angeles. Emphasis is placed on implications for the initiation of community-specific cancer control programs.

Future plans include extending the 1960 and 1970 U.S. data and comparable statistics on Asian Chinese for a two decade trend analysis; exploring the possibility of ascertaining the health status of U.S. Filipinos; initiating field studies on life style changes in relation to cancer control and prevention; and obtaining from the PRC survey and case-control studies data on (1) Soil and water in relation to esophageal cancer; (2) Liver cancer and hepatitis; and (3) Stomach cancer in two high risk areas, with the purpose of testing an innovative statistical method for one set of data.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00114-02 BB

PERIOD COVERED

October 1, 1984 to September 30, 1985

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)

Morbidity Among Long-Term Survivors of Childhood Cancer and Their Offspring

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

PI:	M. H. Myers	Mathematical Statistician	BB, DCPC, NCI
Others:	J. J. Mulvihill	Chief	CGS, CEB, DCE, NCI
	R. R. Connelly	Statistician	BB, DCPC, NCI
	M. D. Naughton	Computer Systems Analyst	SORB, DCPC, NCI

COOPERATING UNITS (if any)

University of Iowa; University of Kansas; University of Texas System Cancer Center; Yale University School of Medicine; California State Department of Health; ORI, Inc.

LAB/BRANCH

Biometry Branch, DCPC and Clinical Epidemiology Branch, DCE

SECTION

Office of the Chief

INSTITUTE AND LOCATION

National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.9	0.1

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither

- ☐ (a1) Minors
- ☒ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

This study, done in collaboration with investigators in the Division of Cancer Etiology was designed to detect the effects of cancer and its treatment on childhood patients who survived to adulthood as well as any effects that might have been transmitted to their offspring. Specific issues for investigation were the occurrence of subsequent primary cancers, quality of life, late morbidity other than cancer and infertility among the cases and cancer and birth defects among offspring. Cases were selected from 5 U.S. cancer registries that had a histologically confirmed malignant neoplasm or brain tumor diagnosed under age 20 years, between 1945 and 1974, who survived at least 5 years after diagnosis, and who reached the age of 21 years. Up to 2 sibling controls were selected for each case with sequential priority given to full blood relationship, same sex, closest in age. Interviewer administered questionnaires were obtained for 2285 (91%) of cases and 3265 (91%) of controls.

Surviving cancer patients more often than their sibling controls reported never having initiated a pregnancy: 45% versus 29% for survivors and controls respectively. Among subjects who reported a pregnancy, the average number of pregnancies was 2.42 for survivors and 2.66 for controls. There were no differences between the groups in the rates of miscarriage (11.1% and 11.5% respectively), still births (0.8% in both groups) or ectopic pregnancies (0.6% and 0.5%).

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CN 00115-02 BB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)
Descriptive Cancer Epidemiology

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

PI:	R. R. Connelly	Statistician	BB, DCPC, NCI

COOPERATING UNITS (if any)

LAB/BRANCH
Biometry Branch, DCPC

SECTION
Biostatistical Methodology and Cancer Control Epidemiology Section

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	0.8	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects
  ☐ (a1) Minors
  ☐ (a2) Interviews

☐ (b) Human tissues

☒ (c) Neither

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

The primary purpose of this project is to describe and evaluate the distribution of cancer occurrence in the United States in terms of age, sex, race, place and time in order to identify subgroups of the population that offer possibilities for mortality reduction through intervention. Cancer incidence and mortality rates are analyzed using biostatistical techniques such as log-linear models or models derived from the multistage theory of carcinogenesis. Incidence data from the SEER Program and mortality data from the National Center for Health Statistics together with other data sources are often the focus of such analyses.

Analysis of incidence rates for pleural and peritoneal mesothelioma in the United States revealed an increase over time for pleural mesothelioma among white males but not for females nor for peritoneal mesothelioma among either sex. Incidence rates were highest in seaboard areas where shipyards have been located. Mortality rates for pleural cancer were elevated in several areas of the country that have had asbestos manufacturing plants or shipyards. Choriocarcinoma incidence rates were recently evaluated based on the total female population and also according to the number of pregnancies in the population, a more appropriate denominator since nearly all trophoblastic tumors are related to conception. After adjustment for age and birth effects, whites demonstrated the lowest rates, with blacks and those of other races being at elevated risk. A recent study of the geographic patterns in nasopharyngeal cancer mortality rates in the United States utilized a system of economic subregions to advantage. The 3,056 counties in the country were grouped into 119 subregions with similar socioeconomic characteristics. For white males, clusters of high death rates along the Gulf Coast and southeast Atlantic Coast were clearly evident at the subregion level but not at the county level.

BEST COPY AVAILABLE

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CN 00116-02 BB

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Statistical Methodology Research

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D.P. Byar	Acting Chief	CDTS, BB, DCPC, NCI
OTHERS:	M.H. Gail	Statistician	CDTS, BB, DCPC, NCI
	D.L. Levin	Senior Investigator	OC, BB, DCPC, NCI
	S. Piantadosi	Medical Staff Fellow	CDTS, BB, DCPC, NCI
	D.K. Corle	Computer Systems Analyst	CDTS, BB, DCPC, NCI
	B. Patterson	Mathematical Statistician	CDTS, BB, DCPC, NCI
	W.Y. Tan	Cancer Expert	CDTS, BB, DCPC, NCI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biometry Branch, DCPC

SECTION
Clinical and Diagnostic Trials Section

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
3.1	2.6	.5

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to conduct research in statistical methods and computer techniques with particular emphasis on those appropriate for analyzing data from clinical, diagnostic, and prevention trials and epidemiologic studies of cancer. Many of the problems studied under this project arise from the consultative activities of the Section. During the past year major emphasis has been placed on developing an elaborate computer program for projection of cancer incidence and mortality rates into the future (See Project Z01 CN 00142 SORB). Another major area of emphasis has been the initial development of an interactive user-friendly computer program for determining sample sizes for various kinds of experimental designs. For this project, the best existing programs were combined into a single program and dialogue written to elicit the necessary questions from the user to determine which calculations should be performed. Because of the need for an appropriate design for large-scale prevention studies of smoking cessation in heavy smokers, attention was given to the problem of randomization by groups and a satisfactory design with adequate statistical power was developed for a specific project in this area. Work on designs for prevention studies has continued, particularly the investigation of the new class called partial factorial designs in which certain cells are deliberately omitted from full balanced factorial designs either because of anticipated toxicity or ethical considerations. Work has continued on the problem of missing covariates in non-linear regression models focused on the situations under which estimates of treatment effect may be biased or tests of the null hypothesis may have incorrect statistical size.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CN 00117-02 SORB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Black/White Differences in Cancer Patient Survival

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	Lillian Gigliotti, Ph.D.	Acting Chief	HPSB, DCPC, NCI
Others:	Jan Howard, Ph.D.	Health Scientist Admin.	HPSB, DCPC, NCI
	Benjamin Hankey, Sc.D	Statistician	SORB, DCPC, NCI
	Max H. Myers, Ph.D.	Statistician	BB, DCPC, NCI

COOPERATING UNITS *(If any)*

Biometry Branch, DCPC
Health Promotion Sciences Branch

LAB/BRANCH
Surveillance and Operations Research Branch

SECTION

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, MD 20892-4200

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.8	1.5	0.3

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

A study of black/white differences in cancer patient survival for cancers of the female breast, colon, urinary bladder, and uterine corpus has been initiated in collaboration with the Health Promotion Sciences Branch, DCPC. Data are being collected on 2,600 patients utilizing three population-based cancer registries with information to be obtained on behavioral and nutritional factors, extent of disease, pathological characteristics of the primary tumor, and treatment.

The period of data collection is January 1, 1985 through December 31, 1986. The purpose of this study is to identify behavioral prognostic factors that explain some part of the black/white survival differences that have been observed for cancers of the breast, corpus, and bladder in SEER data for prior years of diagnosis. The identification of such factors will be of importance in the development of cancer control programs which are based on both risk and prognostic factors.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00118-13 SORB

PERIOD COVERED

October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*

Surveillance, Epidemiology, and End Results (SEER) Program

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

John L. Young, Jr., Dr.P.H., Chief (Principal Investigator)
DAS, SORB, DCPC, NCI

A. J. Asire, M.S., Statistician	M. A. Kruse, Medical Record Librarian
B. J. Cicero, Medical Record Librarian	C. L. Percy, M.S.P.H., Statistician
J. B. Cunningham, Medical Record Librarian	L. A. Ries, M.S., Statistician
J. W. Horm, M.S., Statistician	E. M. Shambaugh, M.A., Statistician

COOPERATING UNITS *(if any)* U. of CA, San Francisco; CT Dept. of Health; Fred Hutchinson Cancer Res. Ctr., Seattle; Res. Corp. of the U. of HI; U. of IA; MI Cancer Found.; N. CA Cancer Pgm; NJ Dept. of Health; Emory U.: C'wealth of Puerto Rico Dept. of Health, IMS, Inc.

LAB/BRANCH

Surveillance and Operations Research Branch

SECTION

Demographic Analysis Section

INSTITUTE AND LOCATION

National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
12	9	3

CHECK APPROPRIATE BOX(ES)

☒ (a) Human subjects ☒ (b) Human tissues ☐ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

Data on cancer patients diagnosed from year of entry into the SEER Program through 1983 were submitted to the NCI by the 11 participants in December 1984. One new registry, the State of New Jersey submitted data for the first time with coverage retrospective to January 1, 1979. The 10 previous participants also supplied follow-up data through December 31, 1983 for all patients diagnosed 1973-82.

Survival rates were characterized by the American Joint Committee on Cancer's stage categories. For many anatomic sites, differences in the survival rates previously noted to be significantly higher for whites than for black patients when considering all stages combined disappeared within individual stage categories. This was due to the generally more favorable stage of disease distribution for white patients. For female breast cancer patients the five-year relative survival rate was 75% for whites versus 63% for blacks. This difference was statistically significant, but was accounted for primarily by those who came to diagnosis with lymph node involvement or direct extension of the tumor to adjacent tissues, i.e. stage III-B. For cancer of the uterine corpus, the anatomic site with the greatest difference in survival between black and white patients, even for stage I disease there was a large, statistically significant difference in five-year relative survival rates, 92% versus 75%. Incidence rates for individual years 1973-81 and for the composite of 1973-77 and 1978-81 were published for each SEER area and each ethnic group represented in the Program. Mortality data for these same time periods were obtained from the National Center for Health Statistics and were published. For 1982, the age-adjusted incidence for all cancer sites combined, both sexes combined was 332.6 per 100,000 population while the age-adjusted mortality was 168.5 per 100,000.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00119-02 BB

PERIOD COVERED
October 1, 1984 to September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Consultation on Clinical Trials and Other Studies

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	D. P. Byar	Acting Chief	CDTS, BB, DCPC, NCI
Others:	M. H. Gail	Statistician	CDTS, BB, DCPC, NCI
	D. L. Levin	Senior Investigator	CDTS, BB, DCPC, NCI
	S. Piantadosi	Medical Staff Fellow	CDTS, BB, DCPC, NCI
	D. K. Corle	Computer Systems Analyst	CDTS, BB, DCPC, NCI
	B. Patterson	Mathematical Statistician	CDTS, BB, DCPC, NCI

COOPERATING UNITS *(if any)*
Division of Cancer Treatment, NCI
Division of Cancer Biology and Diagnosis, NCI

LAB/BRANCH
Biometry Branch, DCPC

SECTION
Clinical and Diagnostic Trials Section

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS	PROFESSIONAL	OTHER
2.1	1.8	.3

CHECK APPROPRIATE BOX(ES)
XX (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
XX (a1) Minors
XX (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is to provide consultative services in statistical and epidemiological methodology in the design, interpretation, and evaluation of clinical trials of diagnosis, treatment, and prevention of cancer and other studies requiring this kind of expertise. For some studies the Section provides full statistical support, including development of detailed study plans, assistance in the design of appropriate study forms, supervision of randomization (for trials) and collection, processing, and editing of data, performance of interim analyses during the progress of the study, preparation of progress reports, final analysis of study data, and collaboration in the preparation of scientific papers.

During the past year the Section has continued to provide full statistical support for the randomized clinical trials of treatment conducted by the Lung Cancer Study Group. In the area of diagnosis, the Section is responsible for maintaining an up-to-date inventory and clinical data for a large serum bank containing information and sera for some 12,000 women including some with breast cancer, some with benign breast disease, and asymptomatic controls. These data are used to evaluate potential biological markers.

Some other important activities under this project include (1) analysis of SEER data for breast and colon cancer to detect geographical areas ("hotspots") where the stage distribution at diagnosis or survival by stage are atypical, (2) analysis of U.S. male lung and prostate cancer mortality maps using regression techniques in order to generate new epidemiological hypotheses concerning possible ecological risk factors, (3) studies of selenium pharmacokinetics needed for possible prevention trials, and (4) a study to estimate population consumption of foods thought to be protective or harmful to cancer risk.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CN 00121-01 BB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Research in Biostatistical Methodology and Mathematical Modeling

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	C. C. Brown	Mathematical Statistician	BB, DCPC, NCI
Others:	D. L. Weed	Senior Staff Fellow	BB, DCPC, NCI
	B. J. Trock	Epidemiologist	BB, DCPC, NCI

COOPERATING UNITS *(if any)*

LAB/BRANCH
Biometry Branch, DCPC

SECTION
Biostatistical Methodology and Cancer Control Epidemiology Section

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.2	1.0	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is the research and development of biostatistical methods and mathematical models appropriate for the analysis of epidemiologic studies related to cancer control and prevention. The various statistical problems studied under this project are derived from the needs of other activities in the Division.

This research includes the development of mathematical models which can be used to predict and evaluate the effect of different intervention strategies. A two-stage model of the carcinogenic process, adapted from a model proposed by Moolgavkar, Venzon, and Knudson for studying the effects of cancer-inhibitory agents such as dietary retinoids is currently being developed and tested. In addition, the Armitage-Doll multistage model is being used to quantify the relationship between cigarette smoking prevalence and lung cancer mortality in the U.S. to estimate the effects of hypothetical changes in the future prevalence of cigarette smoking. The trend of lung cancer mortality is also being analyzed by regression models to project its future course which would be expected without any specific population intervention.

Other methodologic problems under investigation include the modification of logistic regression methods to incorporate knowledge of the sampling rates used in population-based case-control studies of cancer, and development of a set of interactive computer programs which can be used to analyze the trends of cancer rates over time.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER

Z01 CN 00122-01 BB

PERIOD COVERED

October 1, 1984 - September 30, 1985

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)

Development of Cancer Control Epidemiologic Methods

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

PI:	D. L. Weed	Senior Staff Fellow	BB, DCPC, NCI
Others:	B. J. Trock	Epidemiologist	BB, DCPC, NCI

COOPERATING UNITS (if any)

LAB/BRANCH

Biometry Branch, DCPC

SECTION

Biostatistical Methodology and Cancer Control Epidemiology Section

INSTITUTE AND LOCATION

National Cancer Institute, NIH, Bethesda, Maryland 20205

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.25	1.05	0.2

CHECK APPROPRIATE BOX(ES)

☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
- ☐ (a1) Minors
- ☐ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

The development of the methods of cancer control epidemiology has been focused in three areas: 1) studies in causal and preventive inference, 2) studies in causal, preventive and 'mixed' interactions, and 3) studies in selection bias. One inferential issue being examined is the use of inductive and deductive logic in epidemiologic explanation. When four distinct properties of causal and preventive explanations are considered-- their origin, consistency, testability, and permanence-- deductive logic proves superior except for their origin which is not a logical process. The implications for cancer control epidemiology are important: competing hypotheses should be proposed before any study begins; and the choice of the best hypothesis is equivalent to that which has been most rigorously tested. Another inferential issue is that of the relationship of the current causal criteria to explanatory progress and to public health decisions. For purposes of explanation, two categories of criteria emerge: those dependent upon the form of the hypothesis being tested and those independent of it. Studies of causal, preventive and mixed interactions have revealed that the links between biological and statistical models are necessary for scientific progress and that in instances in which multistage and initiation-promotion models of carcinogenesis have been examined, the multiplicative model of statistical interaction is deduced. Nevertheless, the use of the multiplicative model of preventive interaction (and the use of the additive model of causal interaction) as thresholds for public health action is not justified, primarily due to ethical considerations. Studies of selection processes in unexposed occupational populations have revealed these findings: the absence of a primary selective effect on mortality at young ages and the presence of an increased secondary selection effect on cancer mortality for workers with long service durations.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CN 00141-01 SORB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Modeling and Statistical Analysis Related to Cancer Control

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	L. G. Kessler, Sc.D.	Chief	ORS, SORB, DCPC, NCI
Others:	A. R. Feldman, M.D.	Medical Staff Fellow	ORS, SORB, DCPC, NCI
	A. Baranovsky, M.S.	Health Statistician	ORS, SORB, DCPC, NCI
	A. M. Hartman, M.S.	Health Statistician	ORS, SORB, DCPC, NCI
	G. Block, Ph.D.	Staff Fellow	ORS, SORB, DCPC, NCI

COOPERATING UNITS *(if any)*
Smoking, Tobacco and Cancer Program, Diet and Cancer Branch, Cancer Control Applications Branch, Cancer Prevention Studies Branch, Biometry Branch, IMS Inc. (biomedical support contractor)

LAB/BRANCH
Surveillance and Operations Research Branch

SECTION
Operations Research Section

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, MD 20892-4200

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
2.0	2.0	0

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The purpose of this project is the conduct of research and analysis on issues related to cancer prevention and control. The emphasis is on analysis of already existing data bases which can provide insight into important problems in cancer control. The specific problems in this area arise from questions which are not answered in the context of current cancer control research, policy questions which are put to the Division, and as spinoffs of other projects under development in the Division.

One study ongoing prior to the establishment of the Operations Research Section was a major study of multiple primary cancer in the SEER data base. This study will provide a comprehensive resource of the most recent data on the occurrence of multiple primaries. The linkage of certain cancers related to preventable causes is important for cancer control research.

The occurrence of multiple risk factors for cancer is also under study. Using a national probability survey from NCHS, a team of investigators is exploring characteristics related to the prevalence of cancer risk factors.

Using the long historical data from the Connecticut Tumor Registry, the prevalence of all major cancer sites is being investigated. This project will not only produce important original research, but also provide an empirical foundation for programmatic decisions concerning cancer survivor studies.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE

NOTICE OF INTRAMURAL RESEARCH PROJECT

PROJECT NUMBER
Z01 CN 00142-01 SORB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT (80 characters or less. Title must fit on one line between the borders.)
Cancer Control Objectives and Cancer Mortality Projections

PRINCIPAL INVESTIGATOR (List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)

PI:	L. G. Kessler, Sc.D.	Chief	ORS, SORB, DCPC, NCI
Others:	D. L. Levin, M.D.	Senior Investigator	BB, DCPC, NCI
	E. J. Sondik, Ph.D.	Chief,	SORB, DCPC, NCI
	M. H. Gail, M.D., Ph.D.	Statistician	BB, DCE, NCI
	J. Horm, M.S.	Statistician	DAS, SORB, DCPC, NCI
	L. Ries, M.S.	Statistician	DAS, SORB, DCPC, NCI
	D. Eddy, M.D., Ph.D.	Director, HPC	Duke University

COOPERATING UNITS (if any)
Health Policy Center, Duke University
Biometry Branch, DCPC
Biostatistics Branch, DCE

LAB/BRANCH
Surveillance and Operations Research Branch

SECTION
Operations Research Section

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, MD 20892-4200

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.5	1.5	0

CHECK APPROPRIATE BOX(ES)
☐ (a) Human subjects ☐ (b) Human tissues ☒ (c) Neither
☐ (a1) Minors
☐ (a2) Interviews

SUMMARY OF WORK (Use standard unreduced type. Do not exceed the space provided.)

Projecting cancer incidence and mortality rates, and relating those projections to the attainment of national cancer control objectives are the goals of this intramural research project. The project includes development of a computer model which will project cancer incidence and mortality, meshing together the model with a variety of sources of data, and adapting quantitative cancer control objectives to fit the modeling framework.

The NCI staff (principally Dr. Levin) has developed and written a large Fortran program for the NIH DEC-10 computer which is used to project cancer mortality and incidence figures from 1980 through the year 2020. The computer model is based partially on early work by Dr. David Eddy of Duke University. The model incorporates different models for survival from cancer, includes data for 40 separate cancer sites, includes the ability to examine temporal trends in underlying cancer incidence and in mortality from other causes, allows adjustment to 1970 or 1980 U.S. population standards, and produces the calculation of annual incidence and mortality statistics. The crux of the model is the flexibility to analyze the effect of cancer prevention, screening, and treatment activities, in any combination, on cancer mortality.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 CN 00143-01 CPSB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)* Analysis of Long-Term Followup Data from the BCDDP Project

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	C. Carter, Ph.D., M.P.H.	Staff Fellow	CPSB, DCPC, NCI
Others:	M.S. Micozzi, M.D., M.S.	Staff Fellow	CPSB, DCPC, NCI
	A.S. Schatzkin, M.D., Dr. P.H.	Staff Fellow	CPSB, DCPC, NCI
	P.R. Taylor, M.D.	Act. Dep. Br. Chief	CPSB, DCPC, NCI

COOPERATING UNITS *(if any)*
Biometry Branch, DCPC
Environmental Epidemiology Branch, DCE

LAB/BRANCH
Cancer Prevention Studies Branch, DCPC

SECTION

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
0.25	0.25	0

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
☐ (a1) Minors
☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

The BCDDP screening program began in 1973 in 29 centers in 27 widely dispersed geographic areas of the United States. Initial screening was complete on over 280,000 women over a two-year period. From the original 280,000 participants in the screening phase of the BCDDP, approximately 64,000 were selected for 5 years of long-term followup (LTF) beginning in 1978, to assess the biology and natural history of breast disease, and to test hypotheses relating to detection, etiology, and survival. Those selected for LTF included all breast cancer cases found during the screening phase, all benign breast cancer cases, all those recommended for biopsy, and a sample of "normals". The LTF data base will facilitate the exploration of important questions regarding the etiology and natural history of breast cancer. The size of the subcohorts and breadth of data available on them make this population unique. The large number of cases of both breast cancer and benign breast disease with histologic information available should allow particularly useful analyses of several risk factors in relation to these conditions.

The first 5 years of LTF will be completed in all centers by September, 1986. Further follow-up of the LTF subcohorts is anticipated.

Administration of this project and its analysis is a joint effort within the Division of Cancer Prevention and Control by the Cancer Detection Branch, the Cancer Prevention Studies Branch, and the Biometry Branch, in collaboration with the Environmental Epidemiology Branch, Division of Cancer Etiology.

DEPARTMENT OF HEALTH AND HUMAN SERVICES - PUBLIC HEALTH SERVICE **NOTICE OF INTRAMURAL RESEARCH PROJECT**	PROJECT NUMBER Z01 CN 00144-01 CPSB

PERIOD COVERED
October 1, 1984 - September 30, 1985

TITLE OF PROJECT *(80 characters or less. Title must fit on one line between the borders.)*
Lung Cancer Intervention Study Among Yunnan Tin Miners - Feasibility Study

PRINCIPAL INVESTIGATOR *(List other professional personnel below the Principal Investigator.) (Name, title, laboratory, and institute affiliation)*

PI:	A.S. Schatzkin, M.D., Dr.P.H.	Staff Fellow	CPSB, DCPC, NCI
Others:	J.A. Tangrea, M.P.H.	Pharm. Res. Coord.	CPSB, DCPC, NCI
	P.R. Taylor, M.D.	Act. Dep. Br. Chief	CPSB, DCPC, NCI

COOPERATING UNITS *(if any)*

Surveillance and Operations Research Branch, NCI

LAB/BRANCH
Cancer Prevention Studies Branch, DCPC

SECTION

INSTITUTE AND LOCATION
National Cancer Institute, NIH, Bethesda, Maryland

TOTAL MAN-YEARS:	PROFESSIONAL:	OTHER:
1.0	1.0	0

CHECK APPROPRIATE BOX(ES)
☒ (a) Human subjects ☐ (b) Human tissues ☐ (c) Neither
  ☐ (a1) Minors
  ☒ (a2) Interviews

SUMMARY OF WORK *(Use standard unreduced type. Do not exceed the space provided.)*

This pilot study will investigate the feasibility of conducting an intervention trial of micronutrients for the prevention of lung cancer among tin miners in Yunnan, China. The pilot will specifically be looking at general study logistics, ability to identify and recruit miners at high-risk, adherence to pill taking, potential adverse effects from intervention agents, quality control for data and sample collection/analysis, and baseline nutritional status among the miners.

Lung cancer rates are extraordinarily high among these miners. Males $\geq$ 40 years old with underground mining experience have a crude annual incidence of 1240×10^{-5} while miners aged 60-64 have an incidence rate in excess of 2500×10^{-5} annually. While the reasons for these high rates are not completely known, the miners have been exposed to a number of known carcinogens, including tobacco smoke, radon and radon daughters, and arsenic. In addition, dietary intake of several micronutrients are thought to be inadequate.

This study is being conducted by the Cancer Prevention Studies Branch in collaboration with the Department of Epidemiology of the Cancer Institute of the Chinese Academy of Medical Sciences, the Labor Protection Institute of the Yunnan Tin Corporation, and the Surveillance and Operations Research Branch.

☆U.S. GOVERNMENT PRINTING OFFICE:1985 491 292 21278